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OBSERVATIONS ON CHRONIC ENDOMETRITIS

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Chronic endometritis has been a subject of considerable confusion. Though the histological picture of cervical endometritis is well-defined, that of the body of the uterus presents much difficulty. So far as acute inflammation of the corporeal endometrium is concerned, it is rather definitely established, but the chronic variety presents complexities.

According to the modern conception 'chronic endometritis' has the following three characteristic features:

1. *Firstly,* it is a rare, if not altogether impossible affection of the endometrium, because the latter does not lend itself to any chronic inflammation due to the simple tubular character of its glands and to the regular monthly shedding of its superficial layers in the non-pregnant fertile stage of life. 2. *Secondly,* when chronic endometritis is present, it must be associated with some adjacent nidus of infection in order that the chronic inflammatory condition in the endometrium may be maintained for a prolonged period. 3. *Thirdly,* it must exhibit histologically, large number of plasma cells. The presence of these cells in number will differentiate chronic endometritis from an otherwise normal endometrium in the premenstrual stage, where round cells together with glandular hyperplasia, hypertrophy and irregularity, misled Ruge to coin the name 'glandular endometritis' (Shaw, 1941). It will also serve to differentiate it from Olshausen's 'chronic hyperplastic endometritis' which is now recognised as a non-inflammatory condition—metropathica hæmorrhagica of Schroeder (Eden and Lockyer).

In this article, we are recording our observations from a study of the records of the Pathology Department of the Calcutta Medical College, during a period of 20 years from May, 1920 to May 1940. Our object in writing this is to assess how far this present survey fits in with the current conception of chronic endometritis and to suggest what might be done to modify it, if necessary. Only those cases have been included in which pathological findings in the curette material or in the uterine mucosa, are definitely noted down as one or other form of endometritis (corporeal) or where the picture described might suggest it. Thus we have come across the following classes of descriptions:—

(1) *Acute endometritis*: Those reports that depicted acute inflammatory changes or much polymorphonuclear cell infiltration in the endometrium are included under this head.

(2) *Subacute endometritis*: Only those cases have been included here which showed cellular exudate of subacute inflammation in the endometrium.

(3) *Chronic endometritis*: Under this group, reports like 'chronic endometritis', 'chronic inflammatory changes of various degrees', 'cellular exudate of chronic inflammation' or descriptions like "plasma cells in considerable numbers within the endometrium" have been considered. Pictures described as tuberculomas or tuberculous granulation tissues in the endometrium, have also been included here.

(4) *Endometritis*: Here are counted those reports which run simply as 'inflammatory changes in the endometrium' or only as 'picture of endometritis'. Possibly these were meant to be chronic endometritis.

(5) *Simple endometritis*: In this group cases have been described as simple endometritis, presumably the adjective has been used to mean a condition as opposed to being complicated by glandular changes.

(6) *Hypertrophic and hyperplastic endometritis*: A large number of reports has been put down as 'hypertrophic endometritis' and a few as 'hyperplastic endometritis'. Only these have been grouped under this head.

(7) Many curettages have been reported as simply round cell infiltration in the endometrium. It would perhaps, be going too far to assume these to be cases of endometritis but on the other hand, it would be difficult to consider these as normal. These reports are most non-committal in nature but they confuse the reader. Round cell may mean lymphocytes or histiocytes or even plasma cells. If the pathologists have meant by round cell infiltration an abnormal number of the lymphocytic element, the endometrium might have been a normal premenstrual endometrium but if these related to plasma cells then these were cases of chronic endometritis according to the current conception.

Apart from the above eight group of reports, we have got glandular endometritis—4 cases, hypertrophic glandular endometritis—5 cases, endometritis cystica—2 cases, endometritis cystica (polypus)—1 case. Obviously, these last groups, according to our present idea, are not cases of chronic endometritis, the first two representing premenstrual endometrium and the last two—Schroeder's disease.

We are putting down the various pictures described to suggest a condition of chronic endometritis and their number in a tabular form to enable us to see how far they satisfy the criteria laid down for the acceptance of the conditions as chronic endometritis.

CAUSE AND/OR ASSOCIATED CONDITION

	No. of cases recorded	Amenorrhœa followed by bleeding p. v.	Abortion followed by bleeding p. v.	Placental tissue found on histological exam.	Salpingitis and/or oophoritis	Endocervicitis and/or erosion of cervix	Metritis alone	Tuberculous lesion	Polypus	Carcinoma	Fibroid	Procidentia	No. with recorded causal association	No. without recorded causal association
I. Chronic endometritis ..	83	3	6	—	2	5	1	4	7	—	1	1	30	53
II. Endometritis	60	2	2	1	—	3	1	—	—	1	—	—	10	50
III. Simple endometritis ..	5	—	—	—	—	—	—	—	—	—	—	—	—	5
IV. Hypertrophic and/or hyperplastic endometritis ..	44	—	2	1	2	2	—	—	2	—	—	—	9	35
V. Round cell infiltration in endometrium	22	—	2	—	—	—	—	—	—	—	—	—	2	20
VI. Round cell infiltration in the connective tissues of the uterus	9	—	—	—	9	—	—	—	—	—	—	—	9	—
		Obstetrical after-effect.			Repeated infection from some adjacent focus.				Infected new formation.			Others		
TOTAL ..	223	19			29				11			1	60	163

Now as we go through the above table, we find that from rows I—VI all the cases have been accepted by the pathologists as showing some evidence of chronic endometritis. These cases would total 223. So it appears that only eleven cases per year came under chronic endometritis. When we analyse them we find that nineteen cases were due to sepsis as an obstetrical after-effect, either with a history of amenorrhœa or of abortion followed by irregular bleeding per vagina or with definite finding of placental tissue under the microscope. Chronic inflammation of the endometrium under this condition is quite consistent with our modern idea. The retained product or the open wound of the placental site forms the nidus of infection, which then spreads over the uterine mucosa now incapable of naturally and regularly sweeping away its superficial layers along with the infection—due to post-conceptional amenorrhœa.

In the next category, we find that twenty-nine (29) cases are associated definitely with some focus of chronic infection within the pelvic viscera. These were in the tubes or ovaries or cervial mucosa or in the uterine muscle. In addition to these it is, however, conceivable that there might have been some source of infection in the deep basal layers of the endometrium which were not washed out in the menstrual flood and in the interval between the menstrual periods the persisting infection creeped over the endometrium and set up a chronic inflammatory reaction each time anew. In the tuberculous cases, no adjacent foci were recorded, but it is quite possible that the infection could spread each time, as in the above cases from an adjacent permanent lesion.

Similarly, in the third category comprising of eleven cases, we find the association of tumours, which might have got infected and acted as the source of infection each time. In the last category, the single case is associated with procidentia, the low position of the external os with the consequent inflamed cervix might account for the chronic endometritis.

Thus, sixty (60) cases, from among the recorded 223, were associated with conditions which, according to our present concept, might be accepted as giving rise to chronic endometritis. They may also be described as somewhat rare which is quite consistent. But what about the third essential feature of chronic endometritis, *viz.*, exhibition of large number of plasma cells? Only one case was recorded to be so. About 59 cases we are in dark about the presence of plasma cells.

About the rest, *viz.*, 163 (223 less 60) cases recorded as some or other form of chronic endometritis, we find that these do not conform to the three accepted criteria of chronic endometritis and hence, it seems unjustifiable to accept them as such.

So, if we stick to the three points as required by the modern conception of the subject especially the presence of large number of plasma cells, strictly speaking, we find only one case of true chronic endometritis among the 223 cases thus reported. The rest of the cases would appear to be doubtful. From a study of the history of evolution of chronic endometritis, it seems that the only two conditions which might have erroneously crept in among these reports were the 'cystic glandular hyperplasia' and the 'premenstrual endometrium'.

In cystic glandular hyperplasia, the only feature that can convey a false impression of chronic endometritis under the microscope, is the abnormally hyperplastic and cystic condition of the glands, otherwise there is no room for any confusion. In cystic glandular hyperplasia there is no round cell infiltration of the stroma and here the dilated and cystic glands are lined by a regular, clear epithelium with no evidence of secretory material either in the cells or in the lumen.

About the premenstrual endometrium, the round cell infiltration and the bizarre and irregular glands with outpoured secretion into the lumen, can really present a false appearance of a chronically inflamed membrane, and so they did mislead Ruge. In addition, these pseudo-inflammatory characters may be abnormally prominent as in advanced age, multiparity, disordered endocrines, and perhaps, in the formation of a fertilized though unimplanted ovum (Teacher, 1935) where these can all the more be misleading. Indeed, it is very difficult

even for a pathologist with modern ideas to check the temptation of calling material belonging to this group as those of chronic endometritis. Perhaps the terms like 'glandular endometritis', 'hypertrophic glandular endometritis', 'hypertrophic endometritis', 'endometritis with hypertrophic glands' were coined to describe the quantitative variation in these premenstrual characters rather than a qualitative one in the form of many plasma cells.

It is known that among the round cells of these premenstrual endometria, plasma cells are usually absent or only a few are found. It is also known that plasma cells, often (though not always) constitute the bulk of the round cells that appear in the areas of chronic inflammation. Consideration was made of these two factors and it was accepted that unless plasma cells were present in large numbers, simple round cell infiltration could not be accepted as evidence of chronic endometritis. But there may be one fallacy in this. The nature of the predominant wandering cells in an inflamed area, *viz.*, polymorphs, lymphocytes or plasma cells depend on the pH that develops therein (Menkin, 1934). This latter again depends on the resultant of two factors (*i*) the nature of the tissue and (*ii*) the nature of the irritant. Hence, sometimes an irritant giving rise to chronic inflammation in endometrium may bring about in the uterine mucosa such a pH as not to invite these plasma cells—when only the lymphoid cells might form the bulk of the cellular exudate. Indeed, in a few slides of tuberculoma of the endometrium—which is only a specific type of chronic inflammation—we have failed to detect these plasma cells. This indicates that there may be non-specific chronic endometritis, too, which may fail to show plasma cells. In such a condition we shall have to depend on the lymphoid cells mainly. But in that case we will be confronted with the difficulty of spotting out a chronically inflamed membrane from non-inflamed premenstrual endometrium. To obviate this difficulty, we should make it a point to search for signs of chronic inflammation in the endometrium, prior to the premenstrual stage *i.e.*, in the resting period. If in this resting period we find too many lymphoid cells in the superficial layers even without these plasma cells then there might be some justification in accepting these cases as chronic endometritis.

Summary and Conclusion

Twenty years' record from the Pathology Department of the Calcutta Medical College consisting of 223 specimens are studied with regard to the incidence of chronic endometritis. The data have been critically surveyed as to whether these conformed to the accepted ideas of the subject with special reference to the role of plasma cells in chronic endometritis. It appears justifiable to assert that less confusion will result, if in sending materials for and in reporting chronic endometritis, the points above discussed are remembered.

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Teacher J. H.—A Manual of Obstetrical and Gynaecological Pathology. Oxford University Publications, 1935. Fig. 28 and pp. 30.

COMPLETE HEART BLOCK

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In cases where the impulses fail to pass from the auricle to the ventricle, the ventricle continues to beat at a much slower rate than the auricle, independently of the impulses from the sino-auricular node. The bundle then assumes the function of the production of stimulus for contraction at a point just below the block. This condition is called complete heart block (Mackenzie).

During the last ten years, only six cases of complete heart block were observed and the diagnosis was confirmed by electrocardiogram in four cases. A summary of the cases is given below:

Report of the Cases

Case 1. Syphilitic myocarditis with commencing aortic regurgitation. N. P., Hindu male, aged 40 years, was admitted on 30-3-33 with symptoms of congestive heart failure—œdema of the legs and breathlessness on exertion of seven months' duration. Three years back he had low fever with pain in the joints lasting for seven months. He sought admission since his condition was gradually getting worse. *Physical examination*: A moderately nourished individual with œdema of the lower extremities and dyspnœa. Heart was enlarged with the apex beat in the fifth intercostal space in the anterior axillary line. Systolic murmurs in the mitral area and both systolic and diastolic murmurs in the aortic and pulmonary areas were heard over the precordium. Blood pressure 134/70 m.m. of Hg. Liver was enlarged, lungs showed slight congestion and urine, trace of albumin. X-ray showed enlarged heart. Pulse slow (34 to 40 per minute). Blood Wassermann: Strongly positive. Electrocardiogram (Fig. 1) showed complete heart block, arborization block, prolonged S. T. interval and negative T in lead I.

Case 2. Senile myocarditis with atherosclerosis. M.K.R., Hindu male, doctor, aged 60 years, in November 1934 felt his pulse and counted it to be 42 per minute. Blood pressure 130/70 mm. of Hg. By the end of December the blood pressure rose upto 160/60 mm. of Hg. but the pulse rate was constant at 42 per minute. *Physical examination* on 7-1-35 showed an enlarged heart, apex just external to the nipple line, a faint systolic murmur in the mitral area. and a pulse rate of 36 per minute. Blood pressure 170/70 mm. of Hg. Electrocardiogram on 12-1-35 showed complete heart block, bundle branch block type II and low voltage in all leads (Fig. 2). X-ray of the heart showed slight enlargement. For the next three months his blood pressure varied from 142-165 systolic and 52-70 diastolic and the pulse rate was keeping at the constant rate of 40 per minute.

In April 1935, the patient noticed his pulse rate going up (75-80 per minute), and this was confirmed by another doctor and for nearly a month he maintained this high rate without any heart block.

Till November 1936 his pulse rate varied between 60 and 80 per minute and only on two days he showed complete heart block (pulse 42). Blood pressure varied between 130-170 systolic and 40-76 diastolic.

From November 1936 till July 1938 he kept a constant pulse rate of 36 per minute. Blood pressure gradually became

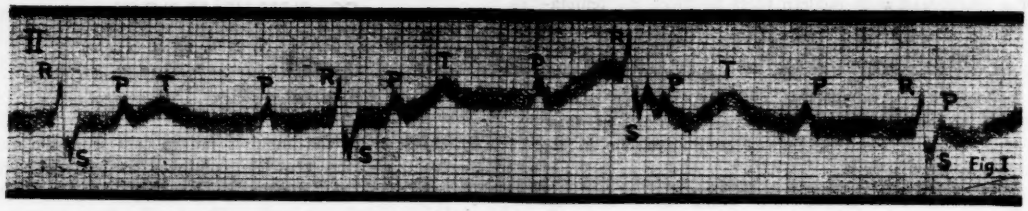

Fig. 1. Lead II (Case 1) showing complete heart block. Seven auricular and four ventricular contractions are seen. QRS is split and its interval is prolonged to 0·12 second showing that there is arborization block in addition to complete heart block. Lead I shows a negative T and ST interval is prolonged to 0·42 to 0·46 of a second.

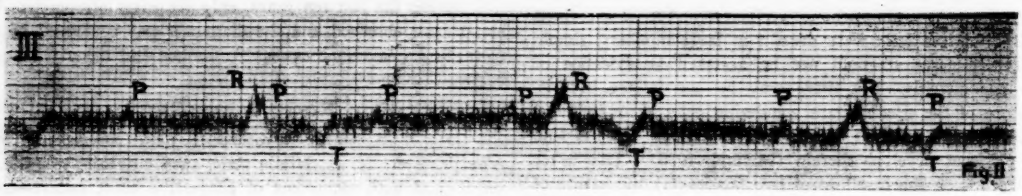

Fig. 2. Lead III (Case 2) showing complete heart block in January 1935. Seven auricular and three ventricular contractions are seen. QRS is split and its interval is prolonged to 0·12 second showing that bundle branch block type II is present in addition. Low voltage present in all leads.

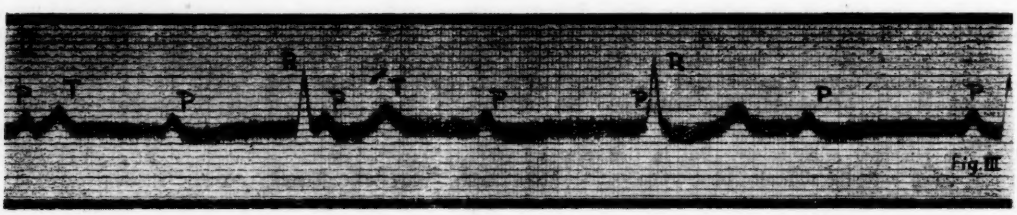

Fig. 3. Lead II. Same case as above showing complete heart block in August 1938. Seven auricular and three ventricular contractions are seen. QRS is normal showing that the previous bundle branch block has disappeared. The low voltage present in the previous plate is absent.

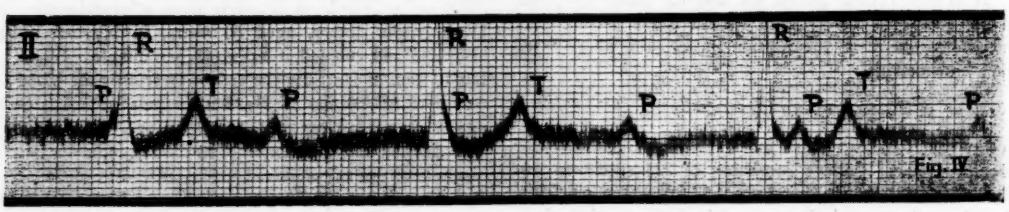

Fig. 4. Lead II. Same case as above showing the effect of 1/50 gr. atropine (after 15 minutes). Four auricular contractions are definitely seen. Two auricular contractions (P) are merged in the R of the first and second ventricular beats. The amplitudes of P, T and R are increased.

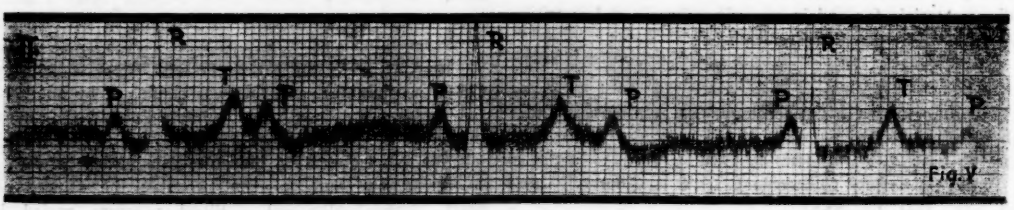

Fig. 5. Lead II. Same case as above showing the effect of 1/50 gr. of atropine (after half an hour). Six auricular and three ventricular contractions are seen. The amplitudes of P, R and T are still increased. The effect of atropine is passing away.

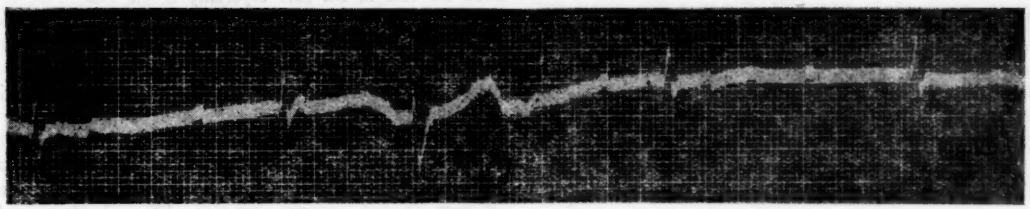

Fig. 6. Lead II (Case 4) showing complete heart block with ventricular extra systole. Seven auricular contractions can be clearly seen, two more are seen of which one is merged with the T of the second ventricular contraction and another with the QRS of the last ventricular beat. Four normal ventricular contractions and one ventricular extra systole are seen. T is flat and low voltage is present in all leads.

high and rose up to 250 systolic but the diastolic was keeping at a low level of 40 mm. He used to take ephedrine without any effect.

In July 1938, he was examined again and he showed a systolic murmur in the mitral area with occasional accentuation of the first sound. Sometimes a third sound due to auricular contraction could be heard at the base of the heart. Pulse rate 35 per minute, not increased by exercise. On looking at the jugular vein, the pulsations were 74 per minute and the dissociation between the auricles and the ventricles could be made out by the simultaneous auscultation at the apex. Blood pressure 190/60 mm. of Hg. Electrocardiogram showed complete heart block and disappearance of the bundle branch block. The cardiac muscle has regained its strength as shown by increase in the amplitude of R in all leads (Fig. 3). Atropine (1/50 gr.) had no effect either on the auricular or ventricular rate (Figs. 4 & 5), but showed increase in the amplitude of both T and R. The maximum effect was observed between 12 to 20 minutes after the injection and the effect passed off after 30 minutes.

Case 3.—Myocarditis of unknown causation. H.M., Hindu male, aged 48 years, was admitted on 9-7-38 with a history of occasional attacks of fainting fits of two years duration. *Physical examination* showed an enlarged heart with systolic murmur and reduplication of the first sound in the mitral area and an occasional third sound at the base, pulse slow, 40-50 per minute—a condition of complete heart block. Blood pressure 140/90 mm. of Hg. Electrocardiogram showed complete heart block. Auricular rate 120. Ventricular rate 48. Another electrocardiogram 3 days later showed an auricular rate of 84 but the ventricular rate remained at 48. Left ventricular preponderance and negative T in leads II and III were observed in addition. Atropine 1/100 gr. did not produce any appreciable increase in either the auricular or ventricular rate, but the amplitudes of P, R and T were increased. T was flat in lead I but negative in leads II and III. He used to get attacks of fainting fits while in hospital for which adrenaline had to be given.

Case 4. A case of myocarditis probably of syphilitic origin. B.S., Hindu male, aged 50 years, was admitted on 14-6-42 with signs of congestive heart failure. Previous history showed nothing of importance. For the last one month he felt exhausted and for the last few days he was getting dyspnœa and slight œdema of the lower extremities. *Physical examination*: a moderately nourished individual. Patient in a condition of dyspnœa; heart—left border 1½" external to the nipple line, systolic and diastolic murmurs were heard in the aortic and pulmonary areas; occasionally a third sound was heard at the base of the heart. Pulse 36 per minute. Jugular pulsation 78 per minute. Blood pressure varied between 160-175 systolic and 55-58 diastolic. Occasional ventricular extra-systoles were heard. Liver enlarged, and tender, spleen not enlarged, moist sounds heard at both bases of the lung behind. Urine—nothing abnormal. Blood Wassermann: strongly positive. Electrocardiogram (Fig. 6) showed complete heart block with ventricular extra systoles. The patient was given diuretics and bromides by mouth and vitamin B_1 injections. Signs of congestive heart failure disappeared. Electrocardiogram taken a second time showed the same picture, but the ventricular extra-systoles disappeared. Atropine 1/100 gr. did not produce any effect either in the rate or in the amplitude. Large doses of atropine were not tried since the patient's condition was very weak.

Case 5. A case of myocarditis probably of syphilitic origin. Mrs. M., Hindu female, aged 40 years, attended the out-patient department in October, 1937, for constipation and vague abdominal pains. Routine examination revealed the condition of complete heart block. Pulse rate 32 per minute and jugular pulsation 72 per minute. Faint systolic murmur was heard in the mitral area. At the base occasionally accentuation of the first sound and sometimes the third sound due to auricular contraction could be heard. Blood pressure 140/90 mm. of Hg. The patient gave a history of syphilis. No other investigation was done since the patient refused to remain in the hospital.

Case 6. A case of myocarditis of unknown causation. A.D., Hindu male, aged 45 years, was admitted on 16-4-39 with signs of congestive heart failure. He gave a history of fits of unconsciousness occurring now and again. His condition became worse during the last two months. *Physical examination* showed a poorly nourished individual. Heart was enlarged, left border in the nipple line and systolic murmur was heard in the mitral and pulmonary areas. Pulse rate 28 per minute and jugular pulsation 64 per minute. Blood pressure 135/75 mm. of Hg. Liver slightly enlarged; other systems were normal. Urine normal. Blood Wassermann: negative. X-ray of the chest showed slight hypertrophy of the left ventricle and dilatation of the ascending aorta. He was discharged on 11-5-39, with his symptoms relieved.

He was readmitted on 2-12-39 with signs of heart failure. Physical examination showed the same condition as above with the exception of blood pressure which was 120/0 (?) diastolic. He was treated with vitamin B_1, iodides and diuretics. Electrocardiogram could not be taken as the machine was out of order.

Discussion

All the cases except one were admitted with some symptom or other. In that case (No. 5) the finding of complete heart block was accidental. Three of the cases (No. 1, 4 and 5) were syphilitic in origin. Two (No. 3 and 6) were due to myocarditis of unknown causation and the case (No. 2) due to senile myocarditis. One of these patients was followed for a period of five years and he could not be traced further.

Mackenzie (1925) observed sixty-four cases of complete heart block and the findings of only 7 cases are given in a summary of 23 cases of heart block. He was able to follow up the cases from 3 months to 11 years. The youngest was 24 and the eldest 80 years. The first case described was observed in 1901 in an old woman of 60 years. She was sent for his opinion as to whether she could withstand an operation for the removal of a big abdominal tumour. The heart was enlarged and the pulse rate 30 per minute. Polygraphic tracing showed complete heart block. This slow pulse rate was observed by a doctor ten years ago after an attack of influenza. Operation was advised and Mackenzie himself gave the chloroform. A huge cyst in connection with the liver was removed with difficulty. The patient was under chloroform for one hour and the pulse of 30 beats per minute was constant during the whole period. Six years later (1907) she was found dead in bed.

Diagnosis

Diagnosis of complete heart block can always be made by the bedside without the aid of the polygraph or electrocardiogram. Simultaneous inspection of the jugular pulsation at the neck, and auscultation at the apex or palpation of the pulse at the wrist will show the auricle contracting regularly with its own rhythm and the ventricle contracting independently of the auricle at the rate of 30 to 50 per minute. Rarely the ventricular rate might go so low as 20 or come up to 60 per minute. The nearer the lesion of the bundle to the auriculo-ventricular node the greater will be the pulse rate. Auscultation will show reduplication of the first sound at the apex or a third sound at the base due to auricular contraction. The pulse rate is not affected by rest or by exercise.

In all the six cases in this series the diagnosis was made clinically and in four cases it was confirmed by electrocardiogram. The pulse varied between 34 and 48 per minute. High pulse pressure was observed in 3 cases. Attacks of fainting fits occurred frequently in one case (No. 5) and injections of adrenaline had to be given to relieve the condition.

Mackenzie (*loc. cit.*) failed to produce any result in complete heart block by the injection of large doses of atropine (1/50-1/30 gr). Very large doses of atropine may cause some increase in the rate especially if the heart rate is high (East and Bain, 1936). The effect of atropine was tried in 3 cases. In one case (No. 4) there was no effect whatsoever but the dose was small (1/100 gr.) In the other two cases there was no increase either in the auricular or ventricular rate but the amplitude of the P, R or T were increased in both the cases. The maximum effect was produced between 15 to 20 minutes and the effect of atropine passed away in half an hour. In another case (No. 3) the auricular rate was different on two separate occasions 120 and 84 per minute. It is evident from this that auricular rate can be affected by outside influence but 1/100 gr. of atropine was not sufficient to increase the auricular rate although the ventricular rate remained at 48 on both occasions. Larger doses of atropine and longer electrocardiographic tracings might show the increase in the auricular rate.

Treatment

Complete heart block in itself does not require any treatment as in case No. 5. Where congestive heart failure is present treatment is necessary and digitalis is indicated. Ephedrine and barium chloride has been tried in cases No. 2 and 3 without any effect. Patient No. 4 showed considerable improvement by injection of vitamin B_1 (5 mg.) first daily and then on alternate days. This drug is recommended in all cases of complete heart block showing signs of heart failure. Syphilitic cases are treated with iodides and mercury by mouth in addition. Adrenaline is indicated in fainting attacks. How adrenaline acts in these cases is not definitely known. Cullis and Dixon (quoted by Mackenzie, *loc. cit.*) were able to demonstrate increased rate of both auricle and ventricle in a rabbit in which complete heart block was produced by cutting the auriculoventricular bundle. The ventricular contractions were stronger than the auricular. Adrenaline was not able to produce any increase in the ventricular rate but the ventricular standstill which brings about the fainting attacks is abolished by it (Mackenzie).

Summary

1. Six cases of complete heart block are described. The diagnosis in four of them was confirmed by electrocardiograms.

2. The effect of atropine was studied in 3 cases.

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East, T. and Bain C.—Recent Advances in Cardiology. J. A. Churchill Ltd. 1936. p. 146.

CAPT. K. L. SAHA GOLD MEDAL

Capt. K. L. Saha, M.B., has offered a gold medal for the best paper on any subject in Pharmacology to be read at the 1944 session of the All-India Medical Conference to be held at Cawnpore during Christmas week.

Research workers and investigators who intend to submit a record of their work on this subject, are requested to send six typed copies of their articles to the Hony. General Secretary, Indian Medical Association, 23, Hindusthan Buildings, Calcutta, so as to reach the latter by the 30th September, 1944.

P. B. Mukerji,
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RESISTANT CASES OF MACROCYTIC ANAEMIAS AND THE PROBLEMS OF THEIR TREATMENT :

A Review of the Present Position

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The ordinary routine treatment of macrocytic anæmias of pregnancy, sprue, pellagra, steatorrhoeas, tropical and other similar varieties of anæmia with liver extracts, marmite high protein diet, and other usual methods is satisfactory in the majority of cases but there are certain resistant cases specially of severe type, which fail to respond to the routine treatment with resultant high mortality which it is our duty to prevent or at least reduce to as low a degree as possible. Bagchi's valuable article on the subject of pregnancy anæmias (*J. Indian M. A.*, May 1943) should be an eye-opener to the profession. He records 107 cases of anæmias of pregnancy treated in the Carmichael Medical College, Calcutta, in four years, out of which 94 were of macrocytic type. The mortality in his worst cases was as high as 47 per cent and on the whole it was no less than 24 per cent. The routine treatment of the cases was liver injections, nourishing diet, iron and transfusions of blood when necessary. I tried to get more details of diet and drugs of these cases but failed to get a response to the enquiry. The mortality in these cases is unusually high. It is granted that the cases admitted into our hospitals are usually in a very advanced and almost in a moribund state but it has to be admitted that the hospital treatment should be as up-to-date and effective as possible and that the statistical and other facilities available to hospital workers should be utilised to find out where our treatment is defective. Research workers in India specially of Calcutta schools have not lagged behind their fellows in other countries either in noting the presence of resistant cases or in doing work of sterling value in evolving the effective therapeusis of such cases and in suggesting a line of action to find the right solution of the problems. Our British colleagues, specially Davidson and his co-workers (1939-42), Miller and Studdert (1942) and others have thrown useful light on the subject and the recent view (Fullerton, 1943) appears to be that cases resistant to refined and crude liver extracts yield to ingestion of whole liver and that there are some unknown hæmopoietic factors in it that do the trick. Other workers like Ungley and James (1934), got very good results with yeast given by mouth. Napier and his co-workers (1936-38) did extensive systematic work on the subject and came to the conclusion (1938) that crude liver and yeast cured resistant cases and that the unknown hæmopoietic factor was probably a member of vitamin B complex.

However, it appears that the advent of liver therapy and its astounding success in cases of Addisonian type of pernicious anæmias would have practically solved the problems of the treatment of the macrocytic anæmias of all varieties had it not been for the nauseating taste and the bulk of the doses of whole liver required for adequate treatment. This disadvantage prompted the introduction of liver extracts which soon gained great popularity because of their ease of administration and rapid results in cases of true Addisonion anæmias. However, it was later on found that refined liver extracts did not give the same uniform results in the treatment of other varieties of macrocytic anæmias. Crude liver extracts were then found to be efficacious for such cases. Some workers then found that yeast did the same work as the crude liver extracts and in some cases even better results were obtained from its use. Nutritional types of macrocytic anæmias were then distinguished and Castle's extrinsic factor in the shape of marmite (yeast) was found giving good result in them. The treatment with refined and crude liver extracts, marmite and high protein diet has been found efficacious but then appeared cases which resisted all the refinements in liver therapy and diet but yielded to ingestion of whole liver by mouth. We, thus, appear to revert to the very same position and stage in liver therapy wherefrom we started first but with the notable addition of the knowledge that there is something in the whole liver which is either inadequate or not at all present in liver extracts and which is also present in yeast and that this something is probably an unidentified member of vitamin B_2 complex. The question, therefore, boils down to the following :—

(1) Cases of macrocytic anæmia resistant to liver extracts, marmite, high-protein and other nourishing diets do exist and are not infrequently met with in general practice.

(2) Such cases generally yield to exhibition of whole liver or yeast by mouth but in cases where absorption of these substances from the gastrointestinal tract is defective or inadequate the response is very protracted and we either have to maintain life for long periods through timely repeated blood transfusions as in Davidson, Davis and Innes' patients or face a very high mortality as in case of pregnancy anæmias reported by workers in India.

(3) The unknown hæmopoietic factor contained in the whole liver or yeast has not yet been identified and attempts to make the extract of yeast or whole liver which may contain this factor in effective quantity have not yet been successful.

(4) Necessity exists for identifying this unknown hæmopoietic factor at an early date in order to make it available for parenteral use in severe cases to save life and avoid protracted illness.

I believe, of course, on clinical grounds, that this member of vitamin B_2 complex is nicotinic acid. I have fully dealt with the subject suggesting the identity of this unknown hæmopoietic factor (nicotinic acid) contained both in the whole liver and yeast that cures macrocytic anæmias refractory to parenteral liver extracts and marmite in a separate paper citing interesting cases, commenting on reported cases and discussing various aspects of my clinical research on the subject in an attempt to give plausible proof of my belief and suggestion. My attention was initially drawn to this subject in 1939 while collecting cases of pellagra detected for the first time in the U.P. by me. I noticed the dramatic effect of anti-pellagra therapy on the hæmopoietic system of one of my cases of secondary pellagra. Nicotinic acid by mouth revived the almost broken system in a marvellous way, making the hyperchromic into hypochromic and macrocytic into normoblastic anæmia in about 20 days.

I continued paying special attention to the subject till at the end of 1940 I got an opportunity of doing a systematic clinical research in order to test the truth of my observations and the relative value of various routine treatments of macrocytic anæmia as compared to nicotinic acid therapy. The result was encouraging. I find that cases of macrocytic anæmias of pregnancy, pellagrous origin, tropical and other varieties which resist all other treatments yield rapidly to nicotinic acid. I have had occasions to fully try all other known methods of

treatment and when every thing failed and the patients were going downhill I, instead of maintaining life by repeated transfusions as Davidson did in his resistant cases, gave nicotinic acid intravenously and got such a ready and rapid response that it was brought home to me with great force that nicotinic acid is a drug to be reckoned with in such cases. A careful study of my own cases and of the available literature has thus made certain things quite evident to me and I have drawn the following conclusions:—

(1) The unknown hæmopoietic factor contained in the whole liver or yeast and which Napier believed to be a member of the vitamin B_2 complex is probably nicotinic acid or a substance which cannot as yet be chemically separated from it.

(2) Resistant type of macrocytic anæmia is not a separate entity but a condition or state of it at which depletion of nicotinamide in the system reaches a degree when the anæmia could yield to no known routine treatment unless the depletion is met with by giving whole liver or medicinal yeast by mouth or pure nicotinic acid per os or parenterally.

(3) The necessity of maintaining life for prolonged periods through timely repeated blood transfusions till one gets a response with whole-liver and other treatments, which is slow to come or in the absence of facilities for such heroic treatment a parentral use of nicotinic acid to avert fatality. The problems of the treatment of macrocytic anæmias of non-Addisonian type appear, therefore, to be varied and confusing due to various causative and other associated factors but as suggested above they seemed to be linked into one system and concern the various stages of one and the same condition. However, the present position is that cases are met with which yield to refined liver extracts like anæmin, others need additional high protein diet, there are still others that respond to crude liver extracts like 'Compolon' while some give way only to yeast and whole liver by mouth and then there do exist cases in which life may have to be maintained with repeated blood transfusions or intravenous nicotinic acid therapy while the drugs given by mouth or liver extracts given parenterally are taking effect.

Davidson and his co-workers (1942) knowing that there are unknown hæmopoietic factors in the whole liver which are not present in the extracts and that when acid peptic and alkaline tryptic digestions are at fault whole liver by mouth cannot be absorbed and is therefore valueless, have made successful attempts to prepare a predigested liver powder which they call 'proteolysed liver'. It is prepared by interaction of whole liver with papain and contains predigested protein material, essential hæmopoietic factors and almost every thing except fats, fat soluble vitamins and undigestible coarse material. The riboflavin concentration is 10 mgms. per 100 gms. of the powder. They hope that it may in time replace the injection treatment of pernicious anæmia and avoid the necessity of whole liver ingestion in resistant cases of macrocytic anæmia of pregnancy, sprue and of other tropical and nutritional deficiency. Their remark that 'it is in the field of refractory anæmias, however, that this preparation may find its most valuable application' makes it evident that it is the puzzling question of the treatment of certain macrocytic anæmias refractory to the usual liver extracts and unsuitable for deriving benefit from whole liver ingestion that has prompted them to try to put up liver in an easily absorbable predigested form. The preparation is still in an experimental stage and is not yet available for general clinical use.

However, the problems relating to the treatment of severe and neglected type of macrocytic anæmias of pregnancy, nutritional and other tropical varieties are of a special concern to the medical profession in India. It is, therefore, necessary to conduct special research on an extensive scale through the co-operation of obstetrical, medical and pathalogical departments of our medical colleges to conclusively prove whether exhibition of whole liver or yeast by mouth in moderately severe and of nicotinic acid intravenously in very severe cases could reduce the mortality or not. The need, at least, a special clinical, for research on the effectiveness or otherwise of nicotinic acid is very great as this is the only available substance at present which could be given intravenously to gain an initial rapid response in those resistant cases in which absorption through gastrointestinal tract is severely interfered with and in some cases not at all present. Dr. John Lowe, the Editor of the *Indian Medical Gazette*, in a personal communication, has recently brought to my notice that there have been several publications on the action of nicotinic acid on macrocyctic anæmia particularly by Italian workers in 1939. This lends an additional strength to my observations and suggestion for a systematic research by workers in India who possess better facilities for the purpose than we have.

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K. S. RAY GOLD MEDAL FOR PAPER ON PUERPERAL SEPSIS

The last date for receipt of papers on Puerperal Sepsis containing a record of original work and investigation on the subject for which a gold medal will be awarded by Dr. K. S. Ray, an ex-President of the I.M.A., to the best worker at the next session of the All-India Medical Conference to be held at Cawnpore during the coming Christmas holidays will be 30th September, 1944. Competitors are requested to send six typed copies of their papers to the undersigned.

23, Hindusthan Building,
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P. B. Mukerji,
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CHEMOTHERAPY OF BACTERIAL INVASION BY ANTI-BACTERIAL SUBSTANCES OF BACTERIA AND MOULDS WITH SPECIAL REFERENCE TO PENICILLIN

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(Continued from previous issue)

The Uses of Penicillin

The dawn of the chemotherapeutic era dates back to the day of salvation of the syphilitic by salvarsan. Sulphanilamide was actually synthesized earlier than salvarsan but its value in bacterial infections became apparent only following the discovery of prontosil. From salvarsan to sulphonamides, from 606 to 693 the unfolding of the story, from treponema to bacteria, has been almost disappointingly slow, although punctuated by developments in divers directions. The progress from prontosil to penicillin, on the other hand, has been phenomenal. Penicillin is no pronoun to prontosil, it professes to be a protagonist in the drama of bacterial chemotherapeusis. It strikes unfortunate, however, that the development of the stage from microbe[1] to mouse,[88] from Fleming to Florey, should be a prolonged one. Fortunately, the scene from mouse[93] to man[94] moved surprisingly quickly, to the relief of millions.

Many human maladies come within the scope of penicillin therapy, and most of the major infections to be feared in the battle front are amenable to it. The supply of penicillin is, unfortunately, still limited due to production difficulties, and the services are having, naturally, a prior claim on the available supplies. Indeed, it is tempting to observe that while the lying-in rooms provided dramatic situations for prontosil, penicillin, it appears, is born to serve the man in the front.

Uses in Bacteriology

Penicillin was born at St. Mary's Hospital, London, and in making this announcement in 1929, Fleming[1] made a special reference to its employment in bacteriological investigations. And at St. Mary's since 1929 special studies have been undertaken for development in that direction. Fleming[1] made the first practical application in 1929 of penicillin to isolate the Pfeiffer's bacillus and ever since it has been used there for that purpose. In 1930 Fleming and Maclean[199] were able to show that hæmophilic bacteria [*H. influenzae* (Pfeiffer) and related organisms] were present normally in all mouths and throats in contrast to variable results of other workers. The success of the work was attributed to the use of penicillin for differential culture, since in a suitable concentration it suppressed the growth of the Gram-positive cocci and *Micrococcus catarrhalis,* while allowing the growth of the influenza group of bacilli. In 1932 Fleming[200] showed that a penicillin-sensitive organism was almost tellurite-resistant and *vice versa;* this observation has been utilised in isolating one species of bacterium from a mixture. For example, sputum was cultured in broth containing a high concentration of penicillin and a low concentration of tellurite. The penicillin inhibited the growth of the Gram-positive cocci, while the tellurite inhibited the para-influenza bacilli and other gram-negative organisms. *H. influenza,* which is slightly less sensitive to tellurite than the para-influenza organisms, grew out in pure culture. Penicillin has also been used to distinguish the saprophytic Gram-negative cocci (*M. flavus*), which are insensitive, from the pathogenic Gram-negative cocci which are highly sensitive. Another of its important uses referred to in 1932 is the demonstration of bacterial inhibitions. For example, a plate was sown with a mixed culture of a streptococcus and *V. cholerae,* and penicillin was spread over half the plate. In the presence of penicillin the streptococcus did not grow, and a pure culture of the *V. cholerae* was found. On the other half of the plate the steptococcus suppressed the growth of the vibrio and was itself found in pure culture. Many similar examples are given.

It is becoming more and more evident that the early bacteriological diagnosis of whooping cough is of the greatest importance in the control of the disease. Maclean in 1937 following a suggestion contained in the first paper on penicillin has used it with great success in the isolation of *B. pertussis.*[201] This may indeed prove to be its most important application in diagnostic bacteriology.

The degree of sensitivity of organisms to penicillin varies, and by carefully grading the strength of penicillin, selective cultures can be made even among the penicillin-sensitive organisms. Thus the acne bacillus, which is only moderately sensitive, has been isolated by Gaddock in 1942, from material in which it is mixed up with the staphylococcus, which is highly sensitive.[202]

These are some of the laboratory uses of penicillin. With its more extensive employment, other useful applications will doubtless appear.

Uses in Clinical Practice

Although it was about 12 years before Florey in 1941 put into effective clinical use the discovery of Fleming in 1929, yet the prize of priority for the first attempt to use it in man must go to Fleming.[1, 200] Fleming employed broth filtrates for 4-hourly irrigation of the conjunctiva and large infected surfaces of man and as a dressing for a number of indolent septic wounds, which "certainly appeared to be superior to dressings containing potent chemicals." Delafield[203] in February 1941 reported the application of penicillin as an antiseptic snuff in nasal infections, Dawson and his associates[204] from the Presbyterian Hospital, N. Y., where investigations on penicillin were commenced closely following the Oxford announcement[93] in 1940, referred briefly for the first time in the U.S.A. to its use in the human subject. This was in May 1941. The first account of the succeeding essays in the clinical field instigated by the *Sir William Dunn* School of Pathology, Oxford, appeared as a part of the second paper by Florey and his colleagues[94] in August 1941.

These were the days when penicillin was being made in the laboratory, and the limited supplies naturally directed attention to utilise such material as was available for chemical and experimental studies. It is, therefore, no surprise that there had been no clinical reports during the remaining part of 1941 and hardly any in 1942. Bodley and his co-workers[205] referred to its use in otorhinolaryngology, and the year 1942 ended with the publication of a report by Herrel, Heilman and Williams[206] from the Mayo Clinic regarding the clinical effectiveness of penicillin which was in agreement with the findings of the Oxford workers[94] published in 1941.

However, an important development occurred in the U.S.A. which foreshadowed future results. When supplies, besides academic output, became available, the Committee on Chemotherapeutic and Other Agents of the National Research Council

was invited in June 1942 to organise and supervise clinical investigations in selected hospitals. The Committee entrusted the work to 22 groups of investigators.[170, 297]

If the year 1942 had proved barren, the year 1943 was rather full. Reports from either side of the Atlantic appeared during the greater part of the year containing observations on different aspects of penicillin therapy. Two reports became available in March. The first from the Mayo Clinic[104] referred to 9 cases comprising chronic ulcers, osteomyelits, cellulitis in and about the face, etc., due to *Staph. aureus* (8) and *Str. hæmolyticus* (1), which were successfully treated by continuous or nearly continuous intravenous administration of penicillin (about 40,000 units/day) excepting 2 cases where local treatment was given, and a case of subacute bacterial endocarditis due to green-producing streptococcus failing to respond. The second one[348] is the second clinical essay from Oxford—after an interval of about 2 years—an interval during which both production and quality of product had been improved. This report in fact laid the foundation of penicillin therapy, and clearly indicated 2 things: that given systemically the drug will control septicaemia or other extensive or dangerous infections due to *Staph. aureus*, and that applied locally it is a perfect antiseptic when circumstances permit its continuous action. Thus local sepsis, in the form of accidental wounds, mastoid and chronic sinuses, was successfully treated by introducing comparatively small amounts of penicillin, as were various superficial infections of the eye. An important outcome of this study is the observation that septic wounds which are to be treated with penicillin must be sewn up in order to retain the solution. This is well illustrated in the new mastoid technique developed by the Floreys. After a Schwartze mastoidectomy the wound was sewn up completely and a fine rubber tube without lateral holes was inserted through the upper end to the base of the cavity. Penicillin was injected 6-hourly, the exudate being aspirated first through the tube before each injection. Treatment was continued for 7 days. Primary union was obtained in 19 instances in a total of 22 of acute, subacute or chronic mastoid infections. This principle in penicillin treatment has been successfully applied in subsequent investigations, e.g., in the treatment of soft tissue wounds in Tunisia[256] or in that of chronic osteomyelitis of the jaw by Mowlem.[244] The results of the earliest trials[64, 142] at Oxford are summarised below:

Recovery	Improvement	Little or no response
143	43	14

The causal organism in the majority of the cases was the staphylococcus, in others it was the streptococcus, or a combined infection by both the organisms. A few infections were pneumococcal, gonococcal or due to actinomyces, and occasionally no organism sensitive to penicillin could be isolated.

From this point the story is taken up elsewhere than in Oxford.

In order to extend and amplify the current knowledge the Medical Research Council, Great Britain, at the request of the Ministry of Supply, appointed in March, a Committee on Clinical Trials of Penicillin which controls the distribution of penicillin for clinical research.[209] In addition to a quantity allocated to the War Office for trials in wounds in Army overseas, supplies of penicillin for research into the systemic and local treatment have been distributed among 8 centres. Clinical reports, about to be described, refer to those mostly coming from sources under the control of 2 Committees, one in the U.S.A. and the other in Great Britain.

The first publication came from a British Centre in May. Dr. Colebrook and his colleagues,[209] working at the Burns Unit at Glasgow, reported about the remarkable effectiveness of penicillin in the form of a cream in eliminating infections from burns. And in the following August came the largest statistical report[176] from America, containing the observations of the 22 groups of investigators appointed by the NRA. The American work, in a way, has confirmed and amplified the British results, mainly in the systemic treatment. However, when it is recalled that the first clinical reference[64] from Oxford included only 5 cases treated by the systemic route, it will not be difficult to appreciate that the over-all results in a total of 500 cases obviously put penicillin treatment in a more assured position than it had possessed before. The results of treatment are appended below:

Diagnosis	*No. of cases*	*Recovery or Improvement*	*Death*	*No effect*
1. Staphylococcus aureus infections ..	228			
With bacteremia	91	54	34	3
Without bacteremia ..	137	109	11	17
2. Streptococcic infections ..	33			
Hemolytic streptococcus ..	23	13	7	3
Nonhemolytic streptococcus ..	4	0	3	1
Anaerobic Streptococcus ..	6	4	2	—
3. Pneumococcic infections ..	76	45	29	2
4. Subacute bacterial endocarditis ..	17	3	4	10
5. Gonococcic infections	129	129*	—	—
6. Meningococcic infections ..	5	4	1	—
7. Miscellaneous infections ..	12	5	3	4
Totals ..	500	366	94	40

* Four of these cases showed only temporary improvement.

The staphylococcal infections included infections with or without bacteraemia, acute or chronic osteomyelitis (48 in a total of 55 recovered or improved), empyema (7 out of 9 recovered or improved), pneumonia, cellulitis, carbuncles of the lip and face, etc. That there should have been 34 deaths in the septicaemic group may appear disappointing but inadequate or delayed treatment and accompanying complications such as uraemia, cancer, etc., must have influenced the ultimate outcome. Moreover, the fatal cases include 9 cases of endocarditis. The results in 33 cases of sulpha-resistant streptococcal infections, mostly due to *Str. pyogenes*, were generally favourable. Most encouraging in the pneumococcal group is the response of the sulpha-resistant pneumonia to moderate doses—less than 100,000 units given over a period of 2 or 3 days. Six had endocarditis and 5 died. There were 16 deaths among 23 cases of pneumococcal meningitis but most of the fatal cases got too little penicillin and a few again got it intrathecally. The result of treatment in 17 cases of subacute bacterial endocarditis is a story of failure, as was the case with earlier reports,[142, 104] or proved to be so in subsequent investigations during the year.[214] Indeed it seems that endocarditis of whatever kind is an unfavourable field for penicillin treatment. However, if penicillin has proved a dismal failure in subacute bacterial endocarditis, its success in gonorrhœa has been unparalleled. In less than 48 hours cures were obtained with small amounts of penicillin, never exceeding 160,000 units. Mahoney,[170] under whose supervision most of the cases of the Keefer's series were treated made a detailed report in September. An earlier observation[210]

from the Mayo Clinic published in May of the successful treatment of 3 cases of sulpha-resistant gonorrhœa had in fact anticipated these results, and their experience in a total of 14 cases were reported[211] in detail in November. In the same month, Welsey Spink[214] discussed at a meeting of the Central Society of Clinical Research the successful treatment of 5 cases of gonorrhœa, and Major Robinson,[224] USAMC, reported at the Royal Society meeting held on Nov. 9 the cure of 93 cases and 2 failures, one of which responded to a second course,—the follow-up of 30 cases upto 1 month did not show any incidence of recurrence or urethral discharge. From Tunisia Priest[215] reported to the War Office and the MRC that "In all cases (9 sulpha-resistant, 1 untreated) the improvement was dramatic, like the turning of a tap."

In September, a publication[216] from the Johns Hopkins Hospital contains a comparative study of the use of penicillin and tyrothricin in otolaryngology. An earlier report[205] in 1942 has already been referred to. Crowe and his co-workers based their discussion in this case on a bacteriological and clinical study of 118 patients. Sulphonamides have several disadvantages in the local treatment of mastoid, chronic sinuses, etc. Tyrothricin is valuable when used to supplement surgery but lasting cure in chronic cases is not often expected since actual contact with bacteria, an essential condition for its action, is difficult to maintain by repeated irrigations only. Often penicillin proved more effective in those cases because the drug is more soluble and penetrate the tissues more than tyrothricin. Acute sinus infections respond rapidly to tyrothricin, however. The difference in the treatment of acute and chronic infections suggests that the bacteria are nearer the surface in the former but have penetrated deeper into the tissues in the more chronic cases.

In October, Fleming[151] published in detail the successful treatment of a case of streptococcal meningitis, partially reported earlier by the Floreys.[148] The interest lies in the fact that this appears to be the first case to receive penicillin intrathecally in British hands and that partial improvement did occur earlier after intramuscular injections only.

Several reports became available in November. Some of these have already been mentioned. On Nov. 5 at a meeting of the Central Society for Clinical Research, Hageman and others[213] presented a series of 22 cases, the response being generally favourable, especially in 8 out of 9 cases of staphylococcic septicaemia. In the discussion Welsey Spink[214] presented a summary of the results in 38 patients. Noteworthy were the failure of penicillin in subacute bacterial endocarditis (3) and pneumococcic meningitis (2) and its success in gonorrhœa (5) and pneumococcal bacteræmia (1).

A quantity of penicillin, it may be recalled, was allocated to the War Office for trial in the Army overseas. And although Pulvertaft[100] published in September the results of the successful treatment of 15 cases of war wounds, the fuller developments in this direction was not known until Florey[217] related his experiences in the Middle East at a meeting of the Royal Society of Medicine held on Nov. 9, where several other investigators, both British[119, 217, 223] and American[224, 225] made notable contribution to the discussion on penicillin.

Florey spent the summer months in Tunisia, evolving with the help of Army surgeons methods for treating battle wounds to prevent sepsis. This study forms the basis of a report to the War Office and MRC by Prof. H. W. Florey and Brigadier Hugh Cairns.[226] This memorandum published by the War Office is not generally available. Short reviews have, however, appeared in the *Lancet*[227] and *B. M. J.*[228] of Dec. 11, and from these and from the reported discussion of the Royal Society meeting[217] the main observations will be briefly referred to.

The method adopted for treatment of battle wounds of soft tissues consisted in excision of skin edges and of damaged tissue, and complete suture, leaving in the wound cavity several narrow tubes, secured in stab wound incisions bordering the wound, through which penicillin solution was injected subsequently. Primary healing was secured in a large proportion of cases in half the customary times, cases generally being infected and of a nature and extent which must have led to prolonged suppuration and very slow healing had orthodox methods been used. Results at 3 weeks were:

Complete union	Subtotal union	Failure
104	60	7

Functional results appeared to be excellent, even in those cases classified as "subtotal" union of the soft parts. However, in wounds complicated by compound fractures the results (suture when possible and short course of systemic therapy) were not so striking, although it is hoped that better results will follow improved technique. Penetrating brain wounds responded satisfactorily—3 died in a total of 23. Four out of 7 cases of gas gangrene responded to treatment and surgery. Other points of interest will be found discussed later.

Several other reports[130, 211, 212, 229-234] appeared before the close of the year 1943.

Flight-Lieut. Bodenham,[229] Officer in charge of a RAF Burns Unit, in a publication on Dec. 11 reported the successful results of the treatment of 75 burns of a duration of 7 to 180 days which were in complete agreement with those of Colebrook and his colleagues.[209] Earlier, he[230] (as well as Cassel[231]) made reference to its use in the burns of eyelids and conjunctiva. In the Royal Society meeting held on Nov. 9 he related his experiences of treatment of surface wounds (including burns), sinuses and cavities with local application of penicillin in various forms.[218] It was necessary, he emphasised, to secure the best conditions for effective application of the drug.

In view of the large production of penicillin in the U.S.A., American Army experiences have been awaited with interest. And as the year was closing, this became available.

The Office of the Surgeon General, U. S. Army, sponsored a pilot unit for penicillin therapy at Bunshell General Hospital, Brigham, and another at Hallovan General Hospital, Staten Island, N. Y. Both units have functioned as "schools" to train medical officers in penicillin therapy seeking definition of the effectiveness of the drug in surgical infections. The experiences of these trained observers as reported from several general hospitals within the Zone of the Interior have been summarised by Lyons.[136] Results are shown below:

Number	Improved	Died	No effect
209	164	13	32

Cases included bacteraemic and non-bacteraemic cases, mostly due to staphylococcus or streptococcus, putrid and pyogenic lung abscesses, septic compound fractures, etc.

The results in the treatment of acute infections are in keeping with the findings of Keefer and his associates.[170] The inability of the drug to control staphylococcic endocarditis has been confirmed. Four cases of malaria due to *P. vivax* were unaffected by penicillin. In addition to the four recorded failures, two other patients developed recurrent malaria under treatment. Two cases of actinomyces infection treated by the Floreys[148] were

not informative because the dosage was probably inadequate: in 1 case, a streptothrix appeared to be eliminated. In the Keefer's series, out of 3 cases, 1 improved and 2 died. There were 4 cases in the present series which improved under treatment but, as Lyons himself says, further follow-up is necessary. In the treatment of staphylococcic osteomyelitis, Lyons feels, surgical intervention is often necessary whereas a more conservative programme is warranted in infections of flat bones. In general, the response to therapy is conditioned by the susceptibility of the infecting organisms and the pathologic anatomy of the inflammatory process.

But of more interest are the observations in connection with chronic septic battle casualties. The soldier with a chronically infected gunshot fracture presents a complex clinical problem. The degree of nutritional depletion is variable and an extreme instance may take precedence over all factors. The infection is usually polymicrobial and may be latent or active. The anatomic abnormality is irregular, requiring a variety of surgical procedures. An intensive study into the clinical status of these cases has revealed a major deficiency of red blood cells and hæmoglobin. And although an adequate diet alone may establish a positive nitrogen balance in the presence of continuing infection, the synthesis of new proteins and regeneration of red blood cells are dependent on control of infection. Consonant to this observation is the finding that penicillin therapy is associated with improved appetite and effective repair of hæmoglobin deficits. But economy of penicillin and hospitalisation requires a supplementary source, preferably whole blood transfusion. The response to penicillin as well as the polymicrobial character of the septic gunshot fractures will be evident from the following:

Type of infection	*Penicillin Response*	
	Systemic	*Local*
I. Putrid		
1. Proteolytic clostridia ..	+ (Large dosage)	+
2. Proteus bacilli ..	0	0
3. Nonhemolytic streptococcus		
a. Mesophillic ..	+	+
b. Thermophillic (Strep. faecalis)	0	0 (or slight)
II. Staphylococcus ..	+ (3-5 days)	+ (often necessary)
III. Hemolytic strepto. ..	+ (1-3 days)	+ (not essential)
IV. Ps. pyocyaneus ..	0	0

The 'unsteady state' of these patients is a severe handicap to the surgeons. However, penicillin therapy has a definite place in the management of these cases. Lyons concludes:

Penicillin therapy permits a direct and immediate approach to the management of septic gunshot fractures. Its role in this regard is analogous to the use of vitamin K for patients with obstructive jaundice. Such a concept emphasises the limitations of penicillin therapy and designates the supplemental position of penicillin in overall surgical program.

This report from Major Champ Lyons closes the year 1943. The year has been richly informative: its sources of fulfilment were foreshadowed in 1942, and, naturally enough, the richness of enquiry and information it has to offer can only be appreciated in its entirety in the year to follow. And truly, 1944 bears the reflection.

If the chronically septic wounds of the soldier presented a clinical problem for study, the control of sepsis of the industrial injuries of the labourers who feed the man at the front has not escaped attention. The results of healing of wounds have in the last analysis to be judged by the return of function; and, obviously enough, the retention of digits and restoration of function are particularly valuable assets in an industrial community where early return to work depends on full use of the hands. And in 1944, at its very advent, appeared a publication which revealed that an analysis of the complete figures for 35 of the penicillin-treated patients with acute infections of the hand showed a saving of about 1,000 man-days of working time as compared with controls. Acute infection of the hand was chosen by Florey and Williams[235] for this study at the MRC Unit, Birmingham Accident Hospital, because they are common in industry and cause much permanent disability, at best considerable loss of working time. The complicated structure of the hand again permitted observations of the effects of penicillin application on skin, areolar tissue, blood vessels, nerves, muscles, tendons, synovial membranes of the tendon sheath and joints, and bone. A comparative study was made in 212 infections. About half were treated by current methods and the other half by local application of penicillin superimposed on the usual surgical procedures. The great majority of the control patients remained septic for well over a week and nearly three fourths were infected till their wounds healed. In the penicillin treated series sepsis was eliminated within a week. Pus was scanty or absent. Relief of pain and throbbing and improvement in the general condition have been striking, and penicillin has effected great saving in the number of dressings. The mean healing time has been considerably reduced by penicillin, but a few cases have shown undue prolongation of healing. Other factors may have caused this. In bone inflammation penicillin led to rapid rarefaction concurrently with improvement in the clinical condition. Reformation of the bony tissue took place readily. The rapid return of mobility to infected parts was one of the most striking features of the penicillin series, but complete normality was not regained after tendon sheaths had contained pus. Among chronic cases penicillin proved of value in preparing infected surfaces for skin grafting and infected stumps for amputation, and for procuring complete healing for dermatitis.

This communication on hand infections was published in the *Lancet* of Jan. 15; however, a reference[228] to it had already been made at the Royal Society meeting held on Nov. 9, 1943. Two papers antidating this may be briefly referred to: one from Cairns,[236] entitled "Gunshot wounds in the acute stage", includes among other materials, a reference to 17 cases of non-penetrating wounds and 23 with penetrating brain wounds, successfully treated by local application of penicillin (compare Florey and Cairns[229]); the other from the Mayo Clinic[237] refers to the dramatic response obtained in 6 cases with extensive cellulitis of mouth (sulpha-resistant 5), complicated with septicaemia (2).

Closely following this, another paper[238] from the Mayo Clinic recorded the disappearance of a nodular syphiloderm which had resisted all forms of local therapy, after continuous intravenous drip of 20,000 units b.i.d. for 8 days. However, much earlier Mahoney, Arnold and Harris[234] had already reported in 1943 the effects of penicillin on the early lesions of syphilis. Four men with chancres of 8-10 days duration were successfully treated by intramuscular injections of 25,000 units given 4-hourly day and night for 8 days. Some malaise and slight fever were produced and the inguinal lymph glands became painful and tender. No. *T. pallidum* could be found after 16 hours. The confirmation of the results obtained by Mahoney *et al.* will be found in the series of 7 cases treated

by Bloomfield, Rantz and Kirby.[220] In a typical case 200,000 units/day for 5 days were given by intravenous drip. After 14 hours no treponema could be found. There was rapid involution of the chancre and nodes over a period of 10 days. In other cases condylomas have become freed of treponemes in about 12-20 hours. In one case of pale but extensive roseola there was a violent flare-up of all the lesions within a few hours of the start of the treatment—a phenomenon probably analogous to the Herxheimer reaction, sometimes seen after arsphenamine.

It seems clear then that immediate results compared to those obtained after full doses of arsphenamine can be achieved. However, prolonged observations have to be carried out before the treatment with penicillin even of the primary syphilis can be accepted as efficient. A case of syphylis needs at the present estimate about 1,000,000 units in a period of 8 days, an amount sufficient for 8 'overnight' cures in gonorrhœa. However, the same remedy happens to be effective in the both the venereal diseases and that it should so seems too good to be true.

These confirmatory results obtained in syphils were related at a symposium[240] on "Antibiotic Agents". The references to the clinical uses of penicillin in that meeting are in fact reports of the experiences of 3 groups of highly qualified investigators, which take the form of several papers in the March issue of the *Journal of the American Medical Association.*

Dawson and Hobby[181] presented clinical data based on 100 cases whereas Herrel[178] summarised the clinical experience at the Mayo Clinic to date in a total of 62 cases. Bloomfield, Rantz and Kirby[220] related their experiences by many illustrative cases, including the cases of syphilis. The type and the nature of the infections treated are in line with those reported by Keefer at al.[176] All of these authors described the treatment of a variety of infections now recognised to be amenable to this drug with generally favourable results. Indeed Kefeer[240] summarises the whole issue when he said in course of discussion that there is general agreement concerning the diseases in which penicillin is an effective agent. The points about which there is no universal agreement are the questions of dosage, the best method of administration and the duration of treatment. These points will be discussed later in the paper. However, some difference of opinion is expresed about the effects to be obtained in bacterial endocarditis. Two alleged cures are described in one paper,[181] whereas in another[178] the treatment is uniformly a failure. Indeed the picture, as Keefer[240] remarked, is confused. He stated that of the 55 cases reported to the Committee, only 3 are alive after one year of study, and he is familiar with other cases in which even after 20 million units the patients are still ill or have died. He also referred to a report by Loewe and his associates[241] where temporary improvement has been recorded in 7 cases. However, a 8th case (not included in the report) has failed to impress after 8 million units given over a period of 8 weeks. The possibility however remains that in a few cases the improvement may be permanent. Indeed this was the dominant note in the talk of Walter S. Priest.[240] He stated that the adequacy of dosage in some of the early failures in subacute bacterial endocarditis is open to question. His own experience read with that of Dawson and Loewe suggests that something may be accomplished by doses of 150,000 to 200,000 units per day over 2 or more weeks.

During the period before and after Christmas, 1943, influenza appeared to be reaching the proportion of a serious epidemic in and about the city of London. The memory or the knowledge of the pandemic in 1918 naturally awakens interest in any modern drug—unfortunately, there is as yet no evidence to suggest that penicillin will abort the primary infection usually believed to be a virus. Pulmonary infections following influenza would, however, present a serious problem for study. Bennet and Parkes[242] undertook such an investigation in a group of cases—apparently in danger of death—selected cases of utmost severity among the thousands who made a natural recovery from the influenzal attack of 1943. Their observations have been published in March with the authority of the Penicillin Committee, Middlesex Hospital.

The recovery of 4 cases of staphylococcal bronchopneumonia without a death suggests that penicillin is of great value in the treatment of this serious complication. But past experience has been that the staphylococcus is a rare invader of epidemic influenza. However, it is felt, in view of recent increase in staphylococcal infections in general, that this organism may prove highly important in the production of mortality, should there be another influenza pandemic.

The treatment of empyema by local injection has hitherto been a story of failure. The introduction of sulphonamide therapy has provided a new clinical spectacle—in the form of occasional clear pleural exudate which become absorbed without further incident. Bennet and Parkes observe that their investigations go further and suggest that not only does penicillin, by local injection combined with systemic treatment (if necessary), offer the prospect of cure in severe and sulphonamide-resistant cases but that it can even bring about cure without rib-resection in cases where the pleural cavity already contains large quantities of pus.

Tillet *et al.*,[243] again, in a publication in May containing report of the favourable response obtained in a series of 48 cases of lobar pneumonia, emphasised that local penicillin treatment in empyema eliminated the necessity of surgical therapy.

In the *B.M.J.* of April 15 appears a report from one of the centres, established by the Penicillin Clinical Trials Committee, MRC, taking the form of 8 papers in different aspects of the subject. The aim of the centre, as Christe and Garrod[170] put it in the introduction, has been to employ the amounts so as to expand rather than to confirm existing knowledge; conditions such as staphylococcal septicaemia which needs great amounts of penicillin were therefore excluded from the later stages of the trial, and local application was developed as far as practicable. 198 patients were treated by local application and 18 by the systemic route. The cases fall into the following groups:

Skin diseases	77
Wounds of the skin & soft tissues ..	70
Breast abscesses	15
Infections of the mandible	20
Other infections of the bone	34

Two papers deal with the infection of the bone. Mowlem[244] has advanced a conception of the dominant role of the vascular disaster in the causation of bone infection and a technique for the treatment of the osteomyelitis of the jaw based upon this has been described. His practice here is to remove all the affected bone, leaving only perhaps a thin lingual plate to maintain continuity. The wound is now closed completely, having inserted 2 tubes through which the bone cavity can be filled with penicillin solution from above. The adjuvant effect of penicillin has led to the conversion of the original open wound method to a closed one, with all the advantages it confers. In the 16 cases so treated elimination of all penicillin-sensitive organisms, satisfactory soft tissue healing, and good regeneration of the bone have taken place, so that recovery from what had

hitherto been an extremely chronic condition has been effected in an average of 30 days. In 4 cases prophylactic use of penicillin has been apparently successful.

In Robertson's hand[245] the treatment of acute osteomyelitis by the systemic route had the almost uniformly favourable results which have already been reported. The account of attempts to treat chronic bone infections, whether hæmatogenous or due to compound fractures and whether by local application or by the systemic route, constitutes largely a record of failure. The success in Mowlem's hand is clearly the effect of radical removal of the affected bone, and perhaps nothing short of this will provide an answer to chronic osteomyelitis elsewhere; indeed Robertson himself contemplates changes in surgical technique.

The treatment of staphylococcal breast abscesses by Fraser[246] appears to indicate that aspiration of pus and injection of penicillin will sometimes replace operation and hasten recovery. It may be that surgical drainage followed by instillation of penicillin solution by an indwelling catheter to achieve and maintain sterility may prove a better method. Study to this end is being continued by Fraser.

The control of pyogenic infections has always been a predominant problem to surgeons in reconstructive procedures for various types of tissue loss. Baron and Mansfield[247] in their report which deals with cases under treatment in an EMS plastic unit bring out several points in connection with the application of penicillin in plastic surgery.

A new but a promising field for treatment with penicillin has been explored by Roxburgh *et al.*[248] Penicillin has been found to be of obvious value in sycosis barbae, impetigo and blepharitis, and effective in some cases of chronic eczema with secondary infection and in some cases of otitis externa. The cure of impetigo is not unexpected but the effect in sycosis barbae, should longer experience confirm it, will rank high among the minor benefits of the discovery of penicillin.

Specific new applications of penicillin therapy continue to be discovered and will doubtless be increasingly extended with supplies becoming more and more abundant. However, there remains many matters that await further examination and definition, even in instances where the efficacy of penicillin has been proved beyond question. Thus, although in gonorrhœa all reports of the past year or in 1944,[178, 214, 239, 251, 252] agree to its uniform and unique success, the details of treatment has been, even here, a matter of opinion. This calls for an examination of the experiences of the different authors so as to compare and correlate them into a practical definition. Ferguson and Buchholtz[253] seek such a definition in a clinical study of 753 cases of gonorrhœa published in May. Their report is a continuation and combination of 2 previous reports published by Mahoney and others.[170, 211] The sum total of cases treated with the various dosages, as shown in the table below, was 753, of which 29 were failures, a percentage of 4.

Group	No. Treated	No. Cured	No. Failed	No. of Doses	Units per Dose	Total Dosage
A	75	74	1	16	10,000	160,000
B	23	23	0	5	20,000	100,000
C	25	21	4	4	25,000	100,000
D	25	24	1	5	15,000	75,000
E	21	16	5	5	10,000	50,000
F	32	32	0	6	20,000	120,000
G	24	23	1	6	18,750	112,000
H	16	16	0	6	16,666*	100,000
I	387	377	10	6	20,000	80,000
J	39	38	1	6	10,833	65,000
K	86	80	6	6	10,000	60,000

* 1st and 6th 20,000; 4 of 10,000.

The continuous intravenous drip, used by Herrel *et al.*,[210] was replaced, after initial trial, by the intermittent intramuscular injections, a route which has been utilised by most workers. The results were quite satisfactory[170] (*see* group A). However, the period of treatment was too prolonged and too many injections were required. A reduction of the dose-time ratio was then used. The results will be seen in the appended table, of particular import would be that the groups B, F and H showed no failures. It appears from an analysis of the results that 5-6 injections of 20,000 units (3-hourly) intramuscularly are necessary for success (*see* groups B. F & H). Treatment according to group I will be useful when the medication is limited and the number of patients large.

The series of cases reported by different investigators contained, in most instances, references to the treatment of meningitis due to one or the other organism. Certain isolated reports have also appeared during the year showing the success[254] or the failure[255] of penicillin therapy in that condition. But an extensive report containing the successful results obtained in a total of 16 cases of sulpha-resistant pneumococcal meningitis has appeared in the *Lancet* of May 15. The results—there being only 4 deaths—compare favourably with those of Keefer's series[179]—16 deaths in a total of 23. However, the interest of this notable contribution by Cairns and his colleagues[250] lies entirely not in the results achieved but also in the valuable information obtained by studying diffusion into and persistence of penicillin in the cerebrospinal fluid. Administration of 3,000 to 4,000 units locally gave an adequate therapeutic concentration for 24 hours—penicillin injected into ventricles reached the lumbar region and the lumbar injection being followed by spread to the surface of the brain and even to a lesser extent into the ventricles. Most of the cases in the present series were treated by intrathecal injections only, by either or both of the routes already mentioned. Injection into the ventricle is strongly advocated whenever feasible. Reliance on the lumbar route may be followed by the development of a block and consequently failure to reach the cerebral meninges. The fact that a continuous effect can be secured for 24 hours after injection into the theca is doubtless responsible for the remarkable success obtained. As in other forms of local treatment with penicillin the retention of the solution in a closed cavity is a condition making for success.

Penicillin has caught the imagination of the public—any mention to it excites interest. Lately, notices of a therapeutic substance—"Vivicillin," obtained from *Penicillium notatum*, purporting to be a super-penicillin have appeared in the popular press. As matters stand now, any yellow material can be advertised as penicillin. In view of these circumstances as well as of shortage of penicillin an investigation was undertaken in a Military Hospital in England. Tests in vitro failed to demonstrate more than a trace of penicillin, notatin or any other antibacterial substance. Clinical trial on 12 patients showed no therapeutic effect. The serum of patients receiving I.M. injections had no definite bacteriostatic effect against the standard Oxford H-staphylococcus. However, all streptococci, staphylococci and gonococci isolated from the cases treated were found to be penicillin-sensitive. These observations, carried out by Crawford and his coworkers[257] with vivicillin supplied by the firm Watford Chemical Co. Ltd., were communicated in a letter to the editor of the *Lancet* and published in its issue of June 3.

At the close of the half year of 1944 appears a publication which recalls an important decision taken towards the latter part of 1943.

At that time—it was then September 1943—the main fighting in which British Army was engaged was in Italy, and the Army Medical Service, inspired by the result achieved in Tunisia,[220] arranged after agreement with the MRC Penicillin Committee to divert the bulk of the British penicillin production to that war zone. Thereupon the War Office formed a "Penicillin Control Unit", consisting of surgeon, pathologist, and laboratory technicians, whose function it was to distribute the drug among the Army, instruct surgeons in its properties and demonstrate its use, instigate special investigations, and collect results.

And in December 1943, Lieut.-Col. J. S. Jeffrey and Major Scott Thomson, both of the Royal Army Medical Corps, arrived in Italy and set up their laboratory in a forward base hospital at Bari since Eastern Italy was then the chief front of the 8th Army. Later on, it was moved to Western Italy to cope with the fighting around Cassino and beyond.

Supplies of penicillin were regularly flown to Italy and distribution was made personally by Jeffrey and Thomson to 80 centres dealing with battle casualties, and later when abundant supplies became available, the refrigerating vans of the Army Blood Transfusion Unit could be seen constantly visiting operating centres.

At first treatment was confined strictly to battle casualties, but with increasing supplies the scheme was broadened to include other casualties and some medical conditions. The general selection of cases and methods of treatment are given below:

Systemic penicillin (I.M./I.V.)—(a) All fractured femurs; the worst-fractured tibiae; fractures of shoulder and upper humerus; other severe fractures (*e.g.*, pelvis); amputations; severe hand injuries; multiple severe soft tissue wounds. It was advised that such cases should be given a short systemic course of penicillin prophylactically as soon as they reach a base hospital. (*b*) Gas gangrene. (*c*) Late cases with established sepsis—in selected cases. (*d*) Septicaemias—waiting for a positive blood culture in medical cases but not in battle casualties.

Local Penicillin.—Wounds of the chest, head, eyes, face, and soft tissue.

Of the over-all benefit that ensued in the numerous cases there can be no doubt. Apart from the general diminution in the infection rate (which by the way more quickly developed in Italy than in the Middle East—an untreated 24-hour old wound might already show pus), and the probable effect of that on the subsequent mortality, many instances could be recalled where the man's life was beyond question saved because this drug was available. The methods employed are in the main those of Florey and Cairns[220] of whose pioneer work in Tunisia this is a continuation in a larger scale. However, new methods of treatment have also been developed, *e.g.*, a technique for the treatment of infected knee joints. Among battle casualties the commonest serious problem from the point of view of infection is fracture of the femur. This aspect with all its repercussion has been specially investigated. It is true that a certain numbers of femurs will always require amputation when the defect is such that an artificial leg is a better proposition and when there is a major vascular injury. And there is no reason why a few of them should die at all from sepsis when the infective organism happens to be penicillin-sensitive. An investigation in this direction has also given encouraging results. Further, with penicillin controlling infection it proved possible to perform definitive amputations of the lower leg in contrast to the current practice in war surgery of amputation and reamputation. The effect of penicillin on several other conditions has been encouraging.

The concerted study of gas gangrene, planned shortly after the war began, found an expression in the papers of MacLennan[240] whose study, classical in its scale and in its thoroughness, undertaken in the Middle East, showed that sulphonamide treatment was disappointing. In view of this information, the therapeutic effect of penicillin in gas gangrene has been awaited with interest, judging by the *in vitro* susceptibility of these organisms and by the results of at least of the prophylactic tests in mice. Reports from the Middle East[220] recorded success in 4 of 7 patients; antitoxin administration and excision of all dead tissues were essential. In 2 who died the infection had been arrested and death was caused by toxaemia. Its greatest use would probably be prophylactic. But it was disconcerting to learn that 4 cases developed gas gangrene actually during treatment with penicillin for compound fractures, although Cutler[225] who described the cases in the Royal Society meeting of Nov. 9 felt that penicillin played a large part in the survival of the patients. In that meeting Jeffrey[221] emphasized that, given parenterally, penicillin should prevent the multiplication of the infecting organisms and the spread of infection, but will not prevent absorption of toxin from the gangenous muscle. For this reason, it is auxilliary to, and in no way supersedes, the other two essentials of treatment, *viz.*, radical surgery and large doses of antitoxin. True to his anticipation, encouraging news now comes from Italy. In a total of 33 cases of true gas gangrene (clostridial myositis) with massive involvement of muscle, the predominant organism being *Cl. welchii*, five were adjudged too ill for surgery and quickly died. The other 28 patients had the full treatment of surgery, antiserum and penicillin according to the following schedule:

(1) Radical surgery—excision of muscle, or amputation if necessary.

(2) Gas gangrene antiserum—49,500 units I.V. at operation (polyvalent antiserum, 27,000 *welchii*, 13,500 *septicum*, 9,000 *oedematiens*), followed in 6-8 hours by a further 49,500 units if no clinical improvement, and repeated again when necessary.

(3) Penicillin systemically—25,000 units of sodium penicillin at operation, and a 3 to 5-day course of 15,000 units I.M. 3-hourly—*i.e.*, 120,000 units a day. (Average 380,000 units). There were 7 deaths, due in 3 cases to fulminating toxæmia, and in the other 4 to late secondary effects such as bronchopneumonia and renal failure. This study provided conclusive evidence that penicillin can arrest the progressive myositis, but that nevertheless, radical surgery is still the main factor.

It would indeed be unfortunate to regard the foregoing few lines as any summary of the admirable survey in a little over 3 pages by Jeffrey and Thomson[250] of the experience gained and gathered in Italy in a total of several thousand cases with penicillin amounting to 700,000,000 units.

The survey, entitled 'Penicillin in Battle Casualties," which covers the experience from January to June, 1944, appears in the opening pages of the *British Medical Journal* in its issue of July 1.

(To be concluded)

A PLEA FOR A SLOW RATE OF INJECTION IN INTRAVENOUS WORK*

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Patient X, emaciated and anæmic due to chronic malaria, had a septic sore on the leg, for which he was given 2 c.c. of a watery solution of iodine intravenously. The patient died on the table soon after the injection. What could be the cause of death? Not being present at the injection, it was a surprise to me how such a small injection could cause the patient's death. But it did; similar deaths have occurred after injections of neo-salvarsan and other medicaments.

Nearly every physician has observed sudden and alarming symptoms after intravenous injections; these symptoms are given different names like anaphylactoid, nitritoid, colloido-clastic or hæmoclastic. In the occurrence of these phenomena, fall of blood pressure is the most prominent feature; there is some breaking down of some compensatory mechanism, which maintains the reaction of the blood; its osmotic tension and its viscosity within the narrow limits of normality. It is surprising that many more accidents like the one described above, do not occur, considering the nicety and delicacy with which these balances must be preserved and the comparative ease with which these may be upset. And the one sure way of upsetting these balances is to inject a medicament into a vein with a rapid rate.

It was, however, not until I came across the experiments of Hirshfeld, Hyman and Wagner (1931) that I could understand so clearly the cause of death in a patient after an injection of a small amount of watery iodine solution into a vein. In a paper on the Influence of Velocity on the Response to Intravenous Injection, (*Arch. Int. Med.*, Feb., 1931) they have described a large number of experiments carried out by them on animals (dogs, rabbits, cats and monkeys) with various solutions of different strengths. The substances injected during the course of these experiments included hypotonic (0·1 per cent), isotonic (0·9 per cent) and hypertonic (10 per cent) solutions of sodium chloride, solutions of dextrose of various strengths (5 to 50 per cent), colloids and gels, drugs like caffeine, digitalis. pituitrin, epinephrin, strophanthin, histamine, arsphenamine, coramine, atropine, quinine and biologic fluids like blood and serum.

As the result of a large number of experiments with these medicaments, the authors came to the conclusion that it is the too rapid rate of injections of intravenous solutions that causes the anaphylactoid reaction. Velocity is considered by them to be the chief factor concerned in causing these reactions and hence they apply the term SPEED SHOCK to these reactions. The major symptoms of speed-shock consisted in changes in the blood and in circulatory and respiratory symptoms. In speed-shock the blood pressure falls precipitously; this might be fatal or recovery might speedily ensue

Two typical experiments (out of so many carried out by Hirshfeld and his co-workers), illustrating the effect of velocity on the occurrence of speed-shock may be quoted. (1) An animal received 25 c.c. of the hypotonic (0·1 per cent) solution of sodium chloride, *at the rate of 1 c.c. per minute*, without any effect on the blood pressure, whereas the same animal showed symptoms of speed-shock with a rapid injection of 2 c.c. of the same solution. (2) 10 c.c. of horse serum was infused slowly into guinea-pigs sensitized ten days previously. No evidence of anaphylaxis occurred. Later 0·1 c.c. was injected rapidly and the animals died of typical shock. These and the other experiments by Hirshfeld and his co-workers leave no doubt as to the importance of velocity in producing vasomotor depression and death. "Danger lies much more in speed of administration than the amount transfused" (Marriot and Kekwick, 1940).

The moral is obvious. Intravenous injections, small or large, in bulk or in concentration, should always be given slowly. But what is the standard rate for a slow injection? Hirshfeld and his co-workers (*loc. cit.*) suggest 1 c.c. per minute for amounts smaller than 100 c.c., and 2 or 3 c.c. per minute for amounts over 100 c.c. These figures, they state, should not be regarded as the last word, but are to be regarded as a first attempt to standardize the velocity of intravenous injections. Titus (1928) regards 4 c.c., workers at the Mayo Clinic (Report of the Committee of the Intravenous Therapy) 10 to 20 cc., Osborne 30 cc., and Keith (1929) 30 to 40 cc. per minute as the standard rate. There is thus no uniformity in the definition of a slow injection and it is certain that no single rate can cover all drugs. Hypertonic solutions should be given more slowly than isotonic and large molecules slower than small molecules. Substances like saline and dextrose may be given more rapidly than more active substances like neosalvarsan and these in turn can be given more rapidly than potent substances like histamine and epinephrin. An ideal rate should eliminate the possibility of speed shock and yet allow the drug to give its specific effect

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* Read at the Scientific Section of XX All-India Medical Conference. Ahmedabad, December, 1943.

DR. S. N. SEN GOLD MEDAL

In memory of his deceased son, Dr. S. N. Sen, B.SC., M.B. (Cal.), Kaisar-i-Hind of Jamalpur (Dist. Monghyr) E.I.Ry., has desired us to announce offer of a Gold Medal for the best paper to be read at the 1944 session of the All-India Medical Conference to be held at Cawnpore during Christmas week on "INTESTINAL OBSTRUCTION AND OTHER COMPLICATIONS OF APPENDICITIS, HOW TO PREVENT AND TREAT SUCH COMPLICATIONS AND SAVE THE PATIENTS FROM THE CRUEL SUFFERINGS AND DEATH." The undersigned will be pleased to receive *six* typed copies of articles on the above subject from research workers and investigators. The last date of receipt of papers will be 31-10-44.

23. Hindusthan Buildings,
Calcutta.

P. B. MUKERJI,
Hony. General Secretary,
Indian Medical Association.

FULMINATING TYPES OF GIARDIASIS SIMULATING ASIATIC CHOLERA AND ACUTE BACILLARY DYSENTERY

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Giardia intestinalis has been known to cause "recurrent attacks of diarrhœa with abdominal distension and discomfort which is occasionally accompanied by passage of large quantities of mucus" (Hurst, 1941-42). It "may develop gradually or with an acute onset resembling dysentery" (Cade and Holland, 1919). The onset is, however generally insidious and the condition tends to become chronic (Osler, 1930). "Blood in the stool is not a characteristic feature" (Sajous, 1923). Some, however, entertain doubt as regards the pathogenicity of giardia while admitting that the condition of patients harbouring this flagellate improve with their disappearance on the administration of atebrin. (Ormistone, Taylor, and Wilson, 1942). Giardia is not only pathogenic but is steadily coming to occupy as important a position among the intestinal infections in tropical countries as Entamœba histolytica. This infection, whether in virulence or in the obstinate chronicity or in complications, is no less serious than that caused by Entamœba histolytica; while the latter invades the liver and causes hepatitis and abscess, the former has been found to invade the gall bladder and gives rise to cholecystitis; it has also "been found in the expectoration in cases of gangrene of the lung and of bronchiectasis, and in the exudate of pleurisy" (Osler, 1930).

The following table compiled from the records of the Khulna District Board Laboratory gives the position of giardiasis as compared with amœbiasis particularly in this part of the country. It will be interesting to note that while incidence of infection by Entamœba histolytica is more or less stationary that due to giardia is making rapid strides, and in eight years it has increased four times and has almost overtaken the former. It further appears that like small-pox both giardia and Entamœba histolytica infections have a periodic exacerbation which occurs every fourth year.

TABLE SHOWING INCIDENCE OF ENTAMOEBA HISTOLYTICA & GIARDIA IN SPECIMENS OF STOOLS EXAMINED

Year	*No. of specimens showing Ent. histolytica*	*No. of specimens showing giardia*	*Total specimens examined*	*Percentage of E. histolytica*	*Percentage of giardia*
1936 ..	7	1	50	14	2
1937 ..	4	1	83	4·5	1·2
1938 ..	6	5	95	6·7	5·2
1939 ..	9	1	68	13·2	1·4
1940 ..	8	5	74	10·8	6·7
1941 ..	7	13	80	8·7	16·2
1942 ..	24	21	256	9·3	8·2
1943 ..	36	32	294	12·3	10·9
Total ..	101	79	1000	10·1	7·9

Since the senior writer (Das Gupta, 1939) drew attention to the growing menace from this flagellate, a number of cases of a fulminating type resembling Asiatic cholera or acute bacillary dysentery have come to our notice. Notes on three such cases are given below:

CASE REPORTS

Case 1—M. S., Bengalee, Hindu male, aged 8 years, on 2-9-43 after an ordinary meal went to school where he felt sick and vomiting and purging started at about 2 P.M. He was sent back home where he rapidly passed into a collapsed condition with Hippocratic facies, cold clammy skin, shrivelled and cyanosed fingers, cramps of the calf and abdominal muscles, restlessness, thirst, husky voice and imperceptible radial pulse, and having frequent large rice-water stools and watery vomits—a typical picture of Asiatic cholera. This was his condition at 5 P.M. when he came under our care. There had been no urine after the first motion. An examination of his stool showed the following: Liquid, white, not offensive, mucus not visible to the naked eye, alkaline, pus cells present in fair number, red blood cells a few, vegetative giardia intestinalis present in abundance, bacteria a few.

He was given 2 pints of hypertonic saline intravenously and Atebrin musonate 0·30 gm. I. M. at 8 P.M. The result was dramatic. Apart from the improvement of the general condition which could be accounted for by the saline, he had only one motion at 9 P.M., a yellow liquid stool about 4 oz. A tablet of stovarsol 4 grains was given that night. He passed copious urine and had a good sleep.

3-9-43—No motion, free urination and good appetite. He was given barley water, *dab* water and glucose and two tablets of stovarsol, no more Atebrin having been available.

4-9-43—Passed a good solid stool and was given rice diet. Stovarsol was continued for a week. A second examination of his stool showed no giardia. He had no further trouble.

Case 2—R. M., Bengalee, Hindu male, aged 38 years, was attacked with vomiting and purging in the early hours (2 A.M.) of 5-11-43. The evacuation in the beginning consisted of undigested rice and other articles of food which he took the previous evening. He had seven motions and two vomits between 2 and 4 A.M. He fainted at 4-30 A.M. and the radial pulse could be scarcely felt. Griping in the umbilical region and cramps of the calf muscles were present. There were 16 motions up to 8 A.M.; urine was scanty. No temperature.

Stool examination—Gelatinous, like raw meat juice, offensive, mucus present, alkaline, pus cells abundant, R.B.C. a few, both cystic and vegetative forms of giardia intestinalis present, bacteria in fair number.

He had been suffering from irregular bowels for over six months. He made a rapid recovery under stovarsol, one pill t.i.d.

Case 3—T. M., Bengalee, Hindu male, aged 3 years, a chronic sufferer from intestinal trouble. From the early hours of 8-11-43 he began to pass liquid reddish stools and vomited undigested food. He had a number of motions before he was examined by one of us at 8 A.M. when his pulse was good and there was no temperature, but he was restless and thirsty. Tongue was clean and dry, there was no pain in the abdomen nor any cramp and the urine was not altogether insufficient.

Stool examination—Gelatinous white with reddish tinge, fishy odour, mucus present, alkaline, degenerated leucocytes in fair number, R.B.C. a few, epethilial cells a few, giardia intestinalis, mainly vegetative form present, bactera scarcely seen—non-motile.

The boy showed signs of improvement before any medical aid was given, still he was given Atabrin, ¼ tablet thrice

daily for 2 days, then twice daily for another 2 days and he made an uneventful recovery. In a second examination of his stool a few days later there was no giardia, vegetative or cystic.

Comments—Cases 2 and 3 showed a tendency to spontaneous abatement of symptoms, a characteristic of early cases of giardiasis; without the aid of microscope it was impossible to arrive at a correct diagnosis in any of these cases. Clinically, there was little difference between case 1 and one of cholera. The other two cases too might well have been diagnosed as cholera, while it was simply impossible to differentiate them from bacillary dysentery since in this country we often get cases of acute bacillary dysentery without any temperature.

Summary

Pathogenesis of giardia intestinalis is discussed.

A statistical table of 1,000 specimens of stool examined is given showing the incidence of giardia as compared with Entamœba histolytica and their possible periodic excerbation.

Notes on 3 cases of fulminating types of giardiasis resembling Asiatic cholera and acute bacillary dysentery are given.

Acknowledgment

Our thanks are due to the authorities of the Khulna District Board for the facilities kindly given in studying the records of their laboratory.

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NAPKIN RASH

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Napkin rash, also known as dermatitis simplex, is generally found in infants but very rarely before the age of 3 weeks.

Cooke (1926) after elaborate study of the problem found that the urea of the fæces is split up into uric acid and ammonia by a Gram-positive bacillus. Pritchard (1938) opined that the presence of an excess of ammonia salts in urine is a result of acidosis. Gordon (1940) thinks that the bacteriological theory is most important and observes that besides the Gram-positive bacillus other commensals and pathogenic organisms present on the skin are also responsible for its causation.

In infants, rash in the napkin area with an ammoniacal smell is characteristic and the condition is self limited. Rash is erythematous in nature and sometimes looks measly. There is no pyrexia but soddening of the part results.

Napkin rash should be differentiated from pityriasis versicolor and also from eczema and syphilis.

Treatment

Gordon (1940) advocates local application of tannic acid in alcohol and picric acid. Pritchard (1938) recommended barley water in plenty to drink. For prophylaxis napkin hygiene is most important and Cooke (1926) advocated soaking napkins in lotio hydrarg. perchlor. (1:4,000). I have treated many cases with success by giving by mouth orange juice one teaspoonful every four hours and with plenty of barley water and boiled plain water to drink and in every case the napkins were boiled and the napkin area was dusted with talc powder. Lotio calamine is best for acute cases.

Acknowledgment

I am thankful to Major H. P. Lall, I.M.S., Surgeon, Patna Medical College Hospitals for encouragement and criticism.

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(*Continued from page 320*)

tion adrenalin 1 c.c. should be given I.M. and O_2 inhalation started.

Accessory Aids in Haemostasis

Local styptics like gauze soaked in adrenalin, or solutions of tannic acid or 30 per cent sodium citrate, turpentine oil, or 1 in 10,000 viper venom may help in capillary bleeding from 'small' wounds. Calcium, vitamins K, vitamin C, sufficient soda bicarb by mouth till urine turns alkaline, hæmostatic serum and tissue extracts like mannitol can be employed prophylactically before an operation.

Secondary hæmorrhage occurs mostly in wounds of calves, buttocks and lower third of thighs. Infection is the principal cause. Tremendous constitutional effects are produced. Occasionally a warning of slight bleeding occurs before the actual large one. Even early there is restlessness, pallor, rapid and feeble pulse and great depression. These are explained as due to the infective clot in the affected vessel producing reflex general vasoconstriction. The wound may have acid pus in it. Prompt treatment is required. Tourniquet should be kept hanging on the head side of the bed and attendants warned to apply it at once in case of bleeding. Opinions differ on the safety of tournique. Surgeons against its use contending that the devitalised tissue, around the site of secondary hæmorrhage cannot stand torniquent strangulation without threat of gangrene. However, in the absence of efficient nursing, a tourniquent will safeguard against immediate death.

The bleeding point should be ligated with thin linen tape or very fat soft silk thread; ends of ligatures are left long; they come out in time. Other ligatures will cut through.

The length of vessel found thrombosed should be excised. This will relax the reflex vasospasm. Ergotamine injection also relieves this spasm. If an artery forceps has caught the bleeding point it should be left in the dressings. Usually on first dressing after 24 to 36 hours no further bleeding will occur. 30% sod. cit. solution soaked in gauze is very good styptic and antacid—acid discharge is common in such wounds.

No radiant heat should be applied to the affected limb in the vain attempt to improve circulation. It may lead to gangrene. A technical point to be kept in mind is to ligate the main vein of a limb as well when the artery has to be ligated, as this is likely to prevent gangrene. The limb thereafter should be kept elevated.

MEDICAL PREPAREDNESS SERIES

HAEMORRHAGES AND HOW TO DEAL WITH THEM*

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When bleeding results from evident violence it is called traumatic hæmorrhage as distinct from spontaneous or pathological hæmorrhage which needs minimal or no trauma. The latter type occurs in such conditions as hæmorrhagic diatheses including different types of purpura, deficiency diseases like scurvy, congenital abnormalities like hæmophilia action of toxins as cobra venom, hepatic dysfunction as in jaundice, pathological conditions of blood vessels as aneurysm or infective arteritis in wounds leading to secondary hæmorrhage.

We are dealing at present with traumatic hæmorrhage. A few remarks will be added at the end on secondary hæmorrhage at it pertains to complications of wounds.

Primary hæmorrhage occurs at the time of infliction of violence. Reactionary bleeding occurs within 24 hours resulting from rising blood pressure as traumatic shock is passing off. All other hæmorrhage occurring thereafter is classed secondary. Infective softening of clot or arterial walls is its main cause and occurs 7 to 10 days later in most cases.

Human body contains about one eleventh of its weight as blood. Most constantly total blood volume averages 3000 to 4000 c.c. per square metre of body surface (average adult measures 1·8 square metres). Roughly, an adult has 10 to 12 pints of blood (5 to 6 metres). The corpuscles and plasma are roughly half and half. Blood volume remains very contant in each individual. Maintenance of blood volume is essential to life. Constitutional effects of bleeding vary with the amount and rapidity of blood loss. If half the total volume of blood is rapidly lost death results—while a gradual loss of 80 per cent is recovered from. At extremes of age effect is more serious though, if adequately treated, children recover rapidly. Women bear blood loss better than men. Clinical features of hæmorrhage depend on its extent and type of vessel involved.

Minor blood loss may cause transient weakness while a serious one produces marked anæmia (early noticed in nails, conjunctiva and tongue), asthenia, giddiness and fainting (recurring on effort or exertion), thirst, restlessness, subnormal temperature, feeble and rapid pulse, rapid and sighing respiration and fall in blood pressure. Marked disability is due to depletion of oxygen carrying hæmoglobin, lack of which takes longest to recover. Saline introduced into blood vessels is rapidly lost into the tissue spaces and urine, and is, therefore, ineffective. A fluid which exerts osmotic pressure to retain water inside blood vessels and which possesses viscosity equal to blood so as to maintain by its friction proper blood pressure, is required. These desiderata can be had by giving gum acacia 6 per cent in normal saline but all samples of gum arabic need careful testing for freedom from toxins and further it has no oxygen carrying capacity.

In the treatment of all hæmorrhages it is imperative to arrest bleeding by securing at the earliest moment the site of leak or lesion in the blood vessels and providing anti-shock treatment with rest and morphia. In addition, in cases where the quantity of blood lost is large say about a pint or more or if blood pressure is down to 100 mm. of Hg. or less in an adult, immediate transfusion with compatible blood is needed. Hæmatocrit reading of corpscular volume and hæmoglobin percentage where laboratory facilities of this nature are available render additional help in this decision.

NATURE'S MECHANISM TO ARREST HAEMORRAGE

The blood around the place of opening or tear in the vessel wall coagulates—this clotting is brought about in shed blood by an enzyme thrombin interacting on fibrinogen. These factors are present in blood. Sufficiency of calcium in circulation aided perhaps by thrombokinase liberated from damaged tissue cells accelerates clot formation. This fibrinous clot is replaced by fibrous tissue which determines permanent arrest of hæmorrhage. Where a vessel is cut or torn across, its inner and middle coats retract, contract and narrow the lumen thus contributing in plugging the end. In addition to this an active vascular spasm has been noticed in main arteries, for example, when a whole limb has been torn off in a serious explosion yet the ends of vessels are so spastically narrowed that not more than 2 to 3 ounces of blood may have been lost from the end of the stump left.

In an incompletely divided vessel or where vessels are tethered to tough fibrous structures as in scalp this natural retraction does not occur. In these cases bleeding is prolonged demanding that the surgeon should totally divide the partially cut vessel or ligature bleeding points. Blood coagulation is delayed in diseases like anæmia, jaundice, scurvy or hæmophilia.

The order of *therapeutic* measures to be adopted consists of:—(1) Preliminary or temporary arrest of bleeding and resuscitation of the patient; (2) Local or permanent control of bleeding; and (3) General or constitutional treatment.

Immediate efforts in dealing with a case of hæmorrhage are to institute measures conducive to temporary arrest of bleeding and to put the patient in such a position that further constitutional deterioration does not occur.

This is done by enforcing absolute rest with head low unless the wound involves the head when the position of the body should be flat. If wound is in the scalp or trunk of the body a pad and pressure bandage, and in case of lower or upper limb same application and elevation of the part will reduce or check blood loss. In limbs apply a pad and bandage over the wound with or without a tourniquet. A rubber elastic bandage over a gauze pad applied over bleeding wound is the best method. The use of unsupervised tourniquet has led to gangrene in many cases. If a tourniquet is employed it should not be applied direct to skin. A pad or cloth should be put under it and the exact time of application of tourniquet must be prominently and carefully noted. No tourniquet should be left on for more than an hour and even that may be too long in case of upper limb as nerves there are very susceptible to pressure paralysis.

If hæmorrhage is very brisk and sutures are available, margins of wound should be temporarily stitched over a pack of gauze inside wound. This has staved over immediate fatality from such a torn vessel as common carotid. If an artery forceps is handy and bleeding point obvious it should be clamped and left on with the dressings, for ligature at a more convenient place and time.

The above treatment is to be initiated in a field or street.

Where even temporary hæmostasis has not been attempted it is not safe to give stimulants. But while it is being done sustaining treatment should go on.

* This is the twelfth of a series of articles on War Medicine, A.R.P. and allied subjects which are being published since May 1943.—EDITOR, *J. Indian M. A.*

This includes lowering the head and application of ascending spiral bandages to all the extremities as is done in obstetric practice. These bandages must only be temporarily applied where there is constant supervision. Prolonged use will threaten gangrene.

In serious hæmorrhage administration of oxygen by the conical face mask and of fluids by the intravenous drip method is very helpful. In order of preference whole blood, citrated blood, or 50 per cent or 25 per cent glucose in saline should be started. The quantity and rate depends on the initial depletion of circulation of the patient. The blood pressure reading will serve as valuable indication. In case of plasma from a blood bank or whole blood, a pint may be administered by the rapid method using safeguards. Intravenous administration rapidly of large amounts of solutions of salt or sugar are futile. The fluid leaves circulation into tissue spaces rapidly and this encourages oedema of lungs or diuresis. Not faster than 40 drops per minute should be the rate of intravenous flow. A practical point is here of use. All these intravascular injections should be done through a canula tied into a vein by open exposure. The canula and tubings should be flushed out with 3·8 per cent sterile or autoclaved sodium citrate solution to effectively prevent clot formation at the site of injection or in the canula.

Local or Permanent Control of Haemorrhage

The dictum "None should be allowed to die of hæmorrhage" implies employment of every possible mechanical, physical or even chemical means to arrest bleeding.

A good survey with retraction of wound margins under suitable anæsthesia and good illumination is very helpful. If any splinter or weapon is left penetrating highly vascular parts like thorax, hepatic area or neck, it should not be disturbed till all aseptic and anæsthetic preparations are available. The embedded foreign body may be efficiently blocking vessels likely to bleed. Then under wide exposure of parts proximal and distal to the embedded foreign body the latter is removed anticipating and providing for the arrest of hæmorrhage. By this methodical approach one very often succeeds. Pressure of compressed cotton with suction tube to torn surfaces often controls bleeding from such fragile organs as liver or kidney in which excision is not desirable in the interest of safety to life. For large veins in abdomen or inside the cranial cavity, the same suction tube with a paste of freshly crushed voluntary muscle succeeds in arresting hæmorrhage. In bony tissue firm pressure with gauze usually succeeds temporarily and, if necessary, beeswax may be rubbed in. Bleeding from foramina is checked by plugs of sterile cotton wool or a sterile match-stick or even a gentle crush with sequestrum forceps. The last is likely to lead to necrosis. Arterial or venous bleeding in limbs is readily arrested by ligature with silk or catgut. If contamination is severe catgut is to be preferred. When extensive lacerations of skin and soft parts coexist with miltiple contaminated fractures though main vessels are not damaged one should weigh his judgment very carefully. Primary amputation will in many cases save life ultimately not only by avoiding risk of secondary hæmorrhage from infection but also by eliminating slow persistent infection of devitalised tissues which do not react efficiently after trauma. Chronic infection persists in the wound undermining health inspite of all antibacterial therapy and sustaining treatment leading to death in extensive injuries of this nature.

Needless to say that sufficient sterile sulphonamide or sulphathiazole should be applied in wounds where vessels are ligatured, specially, if contamination by clothing and street dust figured at the time of casualty. Chemotherapy as a valuable adjunct to surgery has now been definitely established. After ligatures of vessels inside extensive wounds, perfect immobilisation of parts affected is essential. Splints, preferably of plaster of Paris, bivalved and elevated will prevent complications. Large vessels in thorax, abdomen and proximal parts of limbs when partially nicked or punctured may be treated by repair (vasculorrhaphy) using paraffined silk and judicious use of heparin. If a smooth nosed artery forceps does arrest hæmorrhage from such a vessel it is safest to leave it in and dress with gauge round it. After 3 days the artery forceps usually works loose and no recurrence of hæmorrhage occurs. This is not an ideal to be practised but a contrivance to be taken advantage of in deep and inaccessible situations like wounds of the inferior vena cava.

General or Constitutional Treatment

Blood transfusion is the ideal treatment for a patient with a large primary hæmorrhage. If a blood bank supply of whole blood or plasma be available it should be used and at least 750 c.c. administered at outset. If previously tested universal donors be available employ them. But do immediate cross matching. When using any saline or glucose or dried plasma use of pyrogen-free water should be made to avoid reactions. Distilled water treated with activated powdered wood charcoal—filtered efficiently through filter paper and sterilised will help in the mofussil.

In all cases of blood transfusion careful cross matching should be done that is taking a drop of blood of donor mixed with two drops of 3·8 per cent sodium citrate solution to prevent coagulation and this is mixed with a drop of serum of the patient (obtained by taking 2 c.c. of patient's venous blood and centrifugalising or allowing it to clot) within 2 to 10 minutes if blood is incompatible red dust like particles in clear serum will stand out to naked eye or under microscope clumps of R.B.C. are seen. If the serum of the patient does not agglutinate the R.B.C. of the donor, it is considered compatible. This process should also be reversed and the citrated blood of the patient should be titrated with a drop of serum of the donor. This is called cross matching. If both ways it is compatible and the donor has already been tested for syphilis and malaria, the blood of donor is drawn by laying him down, putting a sphygmomanometer cuff round his arm and allowing pressure in the cuff to rise till the veins by the anticubital fossa distend. With a vein puncture needle and a piece of rubber tubing attached, we let the blood from vein of donor to pour into a beaker containing 3·8% sod. cit. in proportion of 1 part of citrate solution to 3 parts of proposed blood to be drawn. Clotting is prevented by frequent stirring.

Finally, during performance of blood transfusion time or clinical test should be finally done. First ten c.c. should be injected slowly letting 1 c.c. to flow per minute and another person, a nurse or assistant to call out every minute the pulse rate. If pulse rises in frequency even though restlessness, cyanosis and rigor do not occur, transfusion should be discontinued. (This clinical caution will never lead to a fatality). If reaction sets in by neglect or rapid transfusion of incompatible blood, immediate injection of 1 in 1000 solu-

(Continued at foot of page 318)

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TREATMENT OF TROPICAL MACROCYTIC ANAEMIA

In 1931, Wills[1] suggested the caption of 'tropical macrocytic anæmia' for cases of macrocytic anæmia, occurring in the tropics, which could not be exactly fitted in the category of true pernicious anæmia of Addison's type. These tropical anæmias were found to differ from true pernicious anæmia in several aspects: first, in these there is usually no true achlorhydria; secondly, the chances for complete cure are better; thirdly, there is no tendency to subacute combined degeneration. These cases were chiefly noted in India, the Malaya States, China, Macedonia and in the west coast of Africa. The condition affecting the women in pregnancy and puerperium most frequently is by no means confined to them. It affects nonpregnant women and males as well.

Being closely related to true pernicious anæmia, the condition came to be treated on the same lines as in the former, with parenteral liver therapy and as iron deficiency is practically always co-existent, oral administration of iron in massive doses has been resorted to, along with liver therapy. Blood transfusion has been required at times to tide over an emergent critical period until the patient responds to hæmopoietic treatment.

Though many a case would respond favourably with such measures alone (Mudaliar and Menon[2], Bagchi[3]), it has been realised by various observers that there is a group of cases which are refractory to such treatment (Fullerton[4] and Davidson[5]). Additional measures have been tried, from time to time, to overcome these refractory cases. As early as 1931 Wills treated a group of cases with autolysed yeast product (marmite) alone and found hæmopoietic results comparable to those of liver therapy in true pernicious anæmia. Soon after this, the dietary factors drew attention of various workers in India and abroad. As to the exact nature of the hæmopoietic factor in marmite, there is no unanimity of opinion. Wills[6] herself believed it to be a protein breakdown product of yeast. Others have attempted to identify the factor with vitamin B complex. Ahmed's suggestion in the current issue of the Journal that nicotinic acid may be the factor, deserves close study and further confirmation. The value of nicotinic acid in anæmia has been previously pointed out by some Italian workers.[7]

Several observers have found that cases refractory to parenteral liver therapy respond to whole liver therapy by mouth (Fullerton and others). Crude liver preparation (of campolon type) for parenteral therapy have sometimes given better results than refined preparations of anahæmin type (Napier and Neal Edwards[8], Davidson, *loc. cit.*). These facts have suggested the existence of an essential hæmopoietic factor in whole liver or crude liver preparations, which is not present in refined liver extract preparations. Attempts are being made to prepare for oral therapy whole liver extracts 'predigested liver extracts' which would include this essential hæmopoietic principle. The exact nature of this factor is not yet known nor it is known whether it is in any way related to nicotinic acid or any other component of vitamin B complex.

Davidson (*loc. cit.*) suggests the deficiency of other dietary factors like preteins and calcium. Strauss[9] has found high protein diet useful in these cases. In view of the fact that gastro-intestinal derangements in these cases may interfere with adequate digestion and assimilation of proteins, one may, with advantage, use proteins hydrolysates with vitamins (riboflavine, nicotinic acid and thiamin) such as have been recently prepared by Narayanan and Krishnan[10] for treatment of starvation cases, intravenously. We hope a trial will be soon given to these proteins hydrolysates in the management of these tropical macrocytic anæmias.

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XXI ALL-INDIA MEDICAL CONFERENCE, CAWNPORE

Office: Temple of Service, The Mall, Cawnpore

SCIENTIFIC SECTION

Members of the Cawnpore Branch of the I.M.A. count on the co-operation of the medical profession in India in making the 21st Session of the All-India Medical Conference to be held at Cawnpore during the next Christmas week, a success.

The success of the Scientific Section depends upon the fullest co-operation of members of the profession who can, by contributing papers on subjects of their choice or initiating discussion on current problems, advance existing knowledge or focus attention on particular aspects of medical science. Papers or requests for discussion are invited on the following subjects:—

Surgery, Medicine, Ophthalmology, Diseases of Ear, Nose and Throat, Obstetrics & Gynaecology, Radiology, Pathology & Bacteriology, Tuberculosis, Nutrition and Pediatrics.

R. ROHATGI,
Secretary, Scientific Section

EXHIBITION

It is notified for general information that a Scientific, Medical and Sanitary Exhibition will be held at Cawnpore during the last week of December, 1944, in connection with the XXI All-India Medical Conference. The Exhibition will provide a very valuable and rare opportunity to the manufacturers of drugs and chemicals and distributors of medical, surgical, sanitary, x'ray and medico-electrical appliances for the display of their products to the elite of the medical profession and the general public.

The rent of each stall will be Rs. 100/- for the whole session payable in advance. Additional accommodation can also be provided at extra cost. For further particulars please apply to:—

B. L. ROHATGI,
Exhibition Secretary

CURRENT MEDICAL LITERATURE

Cardiovascular Manifestations in Pernicious Anaemic

Carter and Traut (*Arch. Int. Med.*, **72**:757, 1943) in reviewing the histories of 300 authenticated cases of pernicious anæmia from the standpoint of cadiovascular symptom observe that there were 257 cases with and 43 without cadiovascular manifestations, that in the presence of severe anæmia it is impossible to segregate dependably patients with primary cardiovascular involvement, that all the usual criteria of cardiovascular disease may occur solely as the result of anæmia, that cardiovascular manifestations often occur with hæmatologic decompensation and disappear—after treatment or during a remission and that the examination of the blood is essential for dependable differentiation.

Cerebral Malaria and Malarial Granuloma

Dhaygude and Purandare (*Arch. Path.*, **36**:550. 1943, Ref. *J.A.M.A.*, **124**:533, 1944) secured in the course of fifteen years a record of 97 cases of malaria in which autopsies were performed. In 55 of these malarial parasites were found in the capillaries of the brain. They were diagnosed postmortem as cerebral malaria. Fever and coma were present in 28. Other symptoms were paresis of limbs, aphasia, dysentery, pneumonia, rigidity of the neck and exaggerated jerks. The condition was confused with meningitis. In all 55 cases malarial parasites were found on necropsy. The external appearance of the brain was abnormal in 43 cases. The fact that in the remaining 12 cases the external appearance was normal indicates the necessity of carrying out a microscopic examination of the brain before ruling out cerebral infection. The most common abnormal change was the slaty grey discoloration of the brain substance. Microscopic examination of the section of the brain showed the capillaries to be filled with malarial parasites and their pigment. In 2 cases minute punctiform hæmorrhages were noticed in the subcortical region. In 5 cases subcortical areas of focal necrosis were seen. There was no evidence of glial proliferation. In 10 cases malarial granuloma was present. A typical malarial granuloma exhibits three zones; the older granulomatous nodules do not show these changes. In them a central capillary is surrounded by a mass of nuclei of the neuroglial cells with little of the necrotic material. Plasmodium falciparum was the infecting type of parasite in the cases in which granuloma was noted. In the year of the epidemic only 1 of 15 brains showed malarial granuloma. The reason probably is that granuloma, which indicates a neuroglial response takes some time to be produced and in an epidemic the patients die quickly. It is easy to imagine that the described lesions would provide the pathologic basis for mental disturbances designated as malarial psychosis.

Falciparum Malaria

Most and Meleney (*J.A.M.A.*, **124**:71, 1944) write that unless malaria is considered as a possibility in every case no matter what the symptoms, the disease may be overlooked and may progress to a point at which treatment is of no avail. If the diagnosis of malaria is not made but the condition of the patient progresses unfavourably, specific treatment for malaria should be instituted. Such treatment should not interfere with other diagnostic procedures, cannot hurt the patient and may prevent fatalities, search for parasites being continued. The biologic characteristics of *Plasmodium falciparum* are sufficiently different from the other human malaria parasities to be reflected in the peculiar, often bizarre clinical features and pathology of falciparum malaria. These fundamental differences are: (1) internal sporulation, (2) massive invasiveness and (3) asynchronicity. The clinical features of falciparum malaria may not follow any given pattern. The symptom of onset are most frequently mistaken for infections of the upper respiratory tract and various gastrointestinal disorders. Severe vomiting and diarrhœa and signs or symptoms of cerebral involvement require intensive parenteral treatment.

Atabrine by mouth is recommended in all uncomplicated falciparum infectious. In cases of severe parasitæmia or evidence of visceral localization, atabrine should be given intramuscularly or quinine intravenously. Such treatment must be started early and continued with intensity until there is sufficient clinical improvement to warrant changing treatment by mouth. In coma or predominant cerebral localization, quinine dihydrochloride should be given intravenously every 4 hours with dextrose solution and isotonic solution of sodium chloride. Spinal drainage may be useful in restoring consciousness. Nicotinic acid intravenously is recommended to produce dilatation of ceretral capillaries

Effects of Plasmochin, Atabrine and Quinine on Electrocardiogram

Heimaun and Shapiro (*Brit. Heart J.*, **5**:131, 1943) observed that leads 4R and 4F showed changes of coronary type in a soldier of 22 who complained of precordial pain while taking plasmochin. Convalescent malaria patients showed that plasmochin increased the amplitude of the various deflections, affecting the T wave constantly and the most striking feature in these cases was the effect on the ST segment simulating changes in coronary thrombosis. Atabrine decreased the amplitude of the various deflections, also affecting the T wave most characteristically, restoring the ST segment to the isoelectric level after it had been raised by plasmochin. Quinine had an effect similar to atabrine but to a lesser degree. Thus plasmochin increased the size of the T wave above normal while atabrine and quinine decreased it below normal; plasmochin has an effect on the ST segment but atabrine and quinine have none.

Salivary Amylase and Dental Caries

Turner and Crane (*Science*, **99**:262, 1944, Ref. *J.A.M.A.*, **125**:35, 1944) reports that there exists a clear relationship between salivary amylase and the incidence of dental caries. In order to establish this relationship, the rate of starch hydrolysis by saliva was determined under standard test conditions. In persons without dental caries this hydrolysis required approximately 45 minutes. The saliva of those with 4 to 6 cavities completed hydrolysis within 19 minutes, those with 10 to 12 cavities within 7 minutes and those with 20 to 30 cavities in less than 2 minutes. Without exception the rate of starch hydrolysis increased in direct parallelism with the number of cavities. Of 51 carefully studied cases not one was found in which the salivary starch splitting rate was an exception to the rate. The origin and nature of this qualitative and quantitative increased buccal amylolytic enzyme is now under investigation.

Treatment of Asiatic Cholera with Sulphaguanidine

Huang (*J.A.M.A.*, **125**:23, 1944) in reporting on the very successful treatment of 20 cases of cholera with sulphaguanidine in Kedeilin, China, observes that there was only one death. Most of these cases were labourers and their ages

ranged as follows: 10-20, 2; 20-30, 8; 30-40, 10; 40-50, 1; 50-60, 0; 60-70, 1. The hours for beginning to receive treatment varied greatly: four hours after onset, 1 case; eight hours, 10 cases; twelve hours, 5 cases; eighteen hours, 4 cases; twenty-four hours, 2 cases. The patients were ordered to drink as much water as possible and circulatory stimulants such as camphor water and tincture digitalis were given repeatedly but no other drugs were given during the whole treatment. Dosage of sulphaguanidine employed were as follows: In adults, 3 gm as a first dose and 1 gm every 2 hours for 6 doses; then 1 gm. every 4 hours for one or two days. In a boy of 11 the first dose was 2 gm. and the maintaining dose was 0·75 gm. and in a girl of 6 the first dose was 1·5 gm and the maintaining dose was 0·5 gm. From 3 to 4 hours after the beginning of the treatment the patients showed general improvement. The author maintains that the combined treatment of sulphaguanidine and saline injection will reduce further the mortality of cholera.

Pain After Amputation and its Treatment

White (*J.A.M.A.*, **124**:1031, 1944) gives in the following lines the summary of his observations: 1. Incapacitating pain after amputation may be due either to irritation of end-bulb neuromas in the stump or, in the cases of a phantom limb with persistence of pain and postural sensations, to their projection from the sensory areas of the cerebral cortex. 2. Local pain, burning and tenderness which are confined to the actual stump can be relieved by: (*a*) Chemical or surgical interruption of the regional sympathetic outflow. These relatively minor and non-mutilating procedures are effective in an encouraging proportion of cases, especially when vasoconstriction and sweating are present to an abnormal degree. (*b*) Section of the spinothalamic tract (chordotomy). 3. The peculiar pain and unpleasant postural sensations of the phantom limb will occasionally respond to sympathectomy or chordotomy, especially if the operation is performed at an early date, but these procedures invariably fail when the personality has started to deteriorate from prolonged suffering, introspection and morphine addiction. 4. In treating difficult problems of this sort it must always be borne in mind that any ineffectual and mutilating procedure, by adding another psychic trauma, must inevitably result in further suffering and loss of morale. 5. Experience has taught that a single resection of a neuroma is justifiable if it is definitely tender and the pain can be relieved by infiltration of procaine hydrochloride. Repeated excision of neuromas, neurectomy, reamputation at higher levels and resection of posterior spinal roots consistently fail and should never be used. 6. In the most severe forms of phantom limb pain, where in the past patients have sunk into hopeless invalidism, become morphine addicts or suicides, it may be possible to obtain relief by new types of surgical intervention directed at the highest centres in the brain. These comprise resection of the contralateral postcentral sensory convolution, from which the phantom sensations appear to be projected or bilateral division of the frontal association fibres, which may be effective by freeing the patient of this intense introspection and anxiety. At present both must be regarded as purely experimental procedures, which will require extensive investigation before their therapeutic value can be estimated. The reason for presenting these procedures in their present theoretical stage is to call attention to their possibilities with the hope that they aid in the solution of a hitherto insoluble problem.

NOTES AND NEWS

REFRESHER COURSE IN OBSTETRICS & GYNÆCOLOGY

The Bombay Obstetrics and Gynæcological Society proposes to hold a Refresher Course in Obstetrics and Gynæcology and Infant Welfare about the middle of February, 1945, provided at least 20 doctors intimate before the 31st December, 1944 their willingness to join the course. It is proposed to charge a fee of Rs. 10 per head. The course will comprise of lectures, demonstrations, visits to hospitals and clinical meetings.

COLLEGE OF PHYSICIANS & SURGEONS, BOMBAY

D.O.M.S. Examination—Out of 15 candidates who appeared in June last, the following 5 have passed:—Dev Raj Bhatia, Raj Brahm, Dhirendranath Singh Chowdhary, Ochhavlal Mohanlal Gandhi, and Lakhshmi Chand Kacker.

Final L.D.S., C.P.S. Examination—The following 2 candidates who appeared in June last, have passed:—Vasant Bhalchandra Lele and Sadashiv Laxmanrao Salunkhe.

V.C.O., I.O.R. & NON-COMBATANTS (ENROLLED) WHO FALL SICK ON LEAVE OR SICK LEAVE

1. Before a Viceroy's Commissioned Officer, Indian Other Ranks, or non-combatant (enrolled) is allowed to proceed on leave, he will be informed by the commanding officer of the following:—

(*a*) If he falls sick while on leave he must (except in the case of severe illness) report sick at once to the nearest military medical officer or military hospital.

(*b*) A medical certificate from a civilian or private medical practitioner will not be accepted as entitling him to an extension of leave; and if he remains absent beyond the stated period of his leave on the strength of such a certificate, he will be treated as absent without leave.

(*c*) In the case of severe illness he will obtain a certificate from a Government Civil Surgeon (or in non-British India from a medical officer employed by the State) stating that, owing to the severity of his illness, it is impracticable to transfer him to the nearest or other military hospital. When it is impracticable, in the circumstances, for him to get in touch with a Government Civil Surgeon (or medical officer employed by the State) he may obtain a certificate from an Assistant or Sub-Assistant Surgeon employed in a Government/District Board dispensary. In either case the man concerned is responsible that the certificate is immediately sent to the authority who granted him leave. This authority will send (by telegraph, if necessary) a request to the medical officer or dispensary in question to the effect that the patient should be transferred to a military hospital immediately he is fit to travel.

(*d*) In view of the particular circumstances obtaining in Nepal, Kumaon, certain hill Districts and other remote localities the provisions above will have to be applied with discrimination by officers commanding certain units and in individual instances. In these cases the officers commanding will issue unit orders on the subject based upon their knowledge of the areas in which their men live.

2. The instructions laid down in I.A.O. 779/43 will be strictly carried out. Where this is conscientiously done few cases should arise of V.C.Os. or I.O.Rs. falling seriously ill while on leave.

CORRESPONDENCE

The Editor is not responsible for any views expressed by contributors.—EDITOR.

SELECT BOOKS ON MEDICAL HISTORY

The Editor, *Journal of the I. M. A.*, Calcutta.

Sir,—Book-publishing and book-buying are both in a very primitive stage in India, at least as far as medical books are concerned. Our text-books for all medical subjects (Pre-medical, non-clinical and clinical, as well as for post-graduate studies and for special branches) have to come from abroad. Students, however, know the necessary lists and names and the practitioners get occasional pamphlets advertising new monographs and often read reviews of books in British, American or Indian medical journals. But, the most amazing degree of ignorance is betrayed, even among the members of the great teaching institutions, about the books recently published and available for enriching or enlarging knowledge of medical history. And many libraries, public and private, may be (and are in some cases) suffering from malnutrition due to the lack of a few inspiring works which all members really need and will read and enjoy. Letters and requests come from various parts of India and from different types and grades of doctors asking advice on books for reading and reference in Medical History. The list here appended is only a short one. Not one of these publications is from India and, unfortunately, none of these deal, except in a very cursory manner, with Medicine in India. I am, etc.

D. V. S. REDDY.

I. History of Medicine.

1. A History of Medicine by A Castiglione. Translated into English. $. 8·50 Knapp.
2. Hippocratic Medicine by H. A. Heidal. $. 2·00. Columbia University Press.

II. Medical Classics.

1. Genuine Works of Hippocrates. William and Wilkins, Baltimore, U.S.A., Translated by Adams F. $. 3·00.
2. Representative Selections. Holmes. O.W. $. 1·25. American Book Co., 88, Lexington Avenue, New York.
3. Cardiac Classics. Edited by F. A. Williams. $. 10·00. Mosley.
4. Essays on Maimonides. Edited by S. W. Baron. $. 3·75. Columbia University Press.
5. Oribassius, Latin. (Oslo Edition).

III. Lives of Medical Men.

1. Leaders of Medicine by Kagan. $. 3·00 Bolton Medico-Historical Press.
2. Nobel Prize Winners by Kapplan. $. 1·00. Chicago.
3. Founders of Modern Medicine (Pasteur, Koch, Lister and others by Metchnikoff and others. Translated by Barges. $. 3·00. Walden Publications, New York.
4. Pioneers of Abdominal Surgery by Z. Cope.
5. Famous Men of Science by S. R. Bolton. $. 4·00. Crowell.

IV. Biographies.

1. Doctors Mayo. By H. B. Clapsattle. $. 3·75. University of Minnesota Press.
2. W. H. Welch by Flexner S. and J. T. $. 3·75. Viking.
3. Berkeley Moynihan, Surgeon by D. Batenman. $. 4·00. Macmillan.
4. Life of Sir William Osler by H. Cushing. $. 5·00.
5. R. Virchow by L. Aschoff. $ 1·80. Marks Hoffaman, Hamburg.

V. Special Topics.

1. History of Tropical Medicine by H. H. Scott. 2. Volumes. Arnold & Co., London. 50 sh.
2. History of Pharmacy by Kremers F. and Undang. G. $. 4·50. Lippincot.
3. Story of Dentistry by M. D. K. Bremer. 20 sh. Kimpton, London.
4. The Story of Surgery by H. Graham. $ 3·75. Double day, Doran.
5. The Priests of Lucina (The Story of Obstetrics.) $. 5·00. Little Brown & Co., Beacon Street, Boston.
6. Syphilis in Earlier Days by J. R. Whitlwail. 5 sh. H. K. Lewis, London.
7. Through the Leper Squint. (Leprosy from Prechristian Times) by A. Weymouth. 5 sh. Selwyn and Boulit Paternoster Van. London.
8. Fatal Partners: War and Disease by R. H. Major. $. 5·00. Little Brown & Co., Beacon Street, Boston.
9. The Flame Burns Bright (A Pageant of Hospital History) by P. N. Mills. $ 1·00. Chicago.
10. Medical Work of Knights by E. E. Hume. $. 3·00. John Hopkins Press, Baltimore.
11. History of the Red Cross by Wernet. 3 sh. 6d. Cassell.

VI. Miscellaneous Subjects.

1. Landmarks in Medicine: Laity Lectures given under the auspices of New York Academy of Medicine. $. 2·00. Appleton Century Company, New York.
2. Men against Microbes. 16 sh. Jarrolds, London.
3. This Dynasty of Doctors by R. Trawn. $. 2·50. Bobbs.
4. Doctors & Doctors, Wise & Otherwise. $. 3·50. Dallas.
5. Harvey Cushing—70th Birthday Celebration and Presentation volume. A collection of tributes and essays published by Cushing Society.
6. Flowering of an Idea: Origin and Growth of Johns Hopkins hospital. A drama by A. M. Chesney. Published by Johns Hopkins Press. $. 1·50.
7. I Remember: Autobiography of A Flexner. $. 3·50. Simon and Schuster.
8. As I Remember Him: Biography of R. S. by H. Zinser.

'A B N-61' IN HUMAN MALARIA

The Editor, *Journal of the I. M. A.*, Calcutta.

Sir,—In the issue of the *J. Indian M. A.*, April, 1944, a preliminary report has been published on the action of "A B N-61", on cases of human malaria. Since the year 1940, a formula has been in use in the Benares State hospitals with therapeautic results almost beyond expectation.

Powdered dita-bark (Chhatim) gr. 8. Triphala powder gr. 10. Cinchona febrifuge gr. 2 for a single dose. Administered in powdered form every 4 hours.

Hoping this information might be of some help, in the research work undertaken. I am, etc.

Ramnagar
16-5-44

G. DAS GUPTA,
Chief Medical Officer, Benares State.

NOTE ON THE QUESTION OF NUTRITION AND PUBLIC HEALTH

The Editor, *Journal of the I. M. A.*, Calcutta.

Sir,—The question of nutrition in India is a complicated problem. It has so far not received the importance and the attention that it should have. As a matter of fact, the question has not been studied at all from the Indian point of view. Dr. Aykroyd of Coonoor Laboratory has, no doubt, done some work on the subject but that is very insufficient and is like a drop in the ocean.

The Indian Medical Association has been pointing this out for sometime past, but no heed has so far been paid to it by the authorities. The XVIII All-India Medical Conference held in December 1941 at Hyderabad (Deccan) passed the following resolution on the subject:—

"This Conference draws the attention of the Government as well as the public to the steadily deteriorating physique of the nation caused, amongst other things, by the lack of adequate and nutritive foodstuffs, rendered worse by gross adulteration of the same. The Conference, therefore, calls upon the authorities to appoint a Nutrition Commission to undertake a comprehensive survey of the important articles of diet as consumed by the general public in the different provinces, and to recommend well-planned and balanced diets, suitable for the needs of the people in the different parts of the country, as well as the measures necessary to ensure a supply of the same."

Copies of the resolution were forwarded to various authorities in the land, but there was no response.

The matter has again come into prominence due to the importance given to this problem by the International Food Conference held recently in the U. S. A. and in which India and other countries were represented by official delegations.

Now that the end of War is fairly visible, a talk has started in various places and one often hears and reads of Post-War Reconstruction. In our own province of U. P. a Reconstruction Committee has been appointed with several sub-committees on various subjects and one learns from the papers that the Executive Council of the Governor General of India has also a Committee on Post-War Reconstruction, but the wonder of wonders is that no committee has so far been appointed on the question of nutrition, which is the problem of problems in this country. Whatever recommendations of the Committee or Committees may be resulting in various forms of reconstruction of the economy of this country, they will all hinge on the health of the Nation and that health itself depends on the question of nutrition of the population. No reconstruction of any sort is possible with B_3 quality of the nutrition that an average Indian receives at present. It is well known to everyone that 90% or thereabouts of the Indians live on the verge of starvation and what little they get to eat is insufficient from the scientific point of view or unbalanced from the point of view of nutritional value and thus it is not enough to maintain them in good health, resulting in early deaths particularly of infants and child-bearing mothers.

An important aspect of the Reconstruction is the settling of war-returned soldiers back into peaceful avocations—be it agriculture or any other. Now from their point of view, is it not criminal to place them in positions, where they would not be able to get either enough food or food of quality to maintain themselves or their families and children in decent health? Considering from even this one point of view, it is justifiable to start the study of nutrition now, so as to be ready, when the need arises.

It is well known that the diet of a vast majority of our countrymen is unbalanced. India is a vast country and from the dietary point of view can be divided into several regions. Taking U. P. for instance, it is known that there is difference between the eastern and the western parts of U. P. In the eastern side, people are comparatively poor due to various causes, which we need not go into here and the diet is more and more rice as we proceed further and further towards the eastern parts of the Province. On the other hand, the people on the western side are comparatively better off and the staple diet is wheat, so that the Province can be divided into more or less two regions, requiring separate study.

Then there has been so far no scientific study of food requirements of an Indian in terms of quantities, nor in terms of qualities. Again there has been no study of food requirements from the occupation point of view, for example, the needs of various classes of workers as mechanics, tailors, skilled and unskilled labourers etc., and for men and women separately. Then again we have to go into the energy needs of various types of people as slender, fat, muscularly, active or old eac., and energy needs in terms of body weight or body surface.

In Europe and America, these and similar studies are constantly going on and have resulted in a vast literature on the subject, which has been utilised for improving the health of those countries in various ways, but nobody has ever bothered to do even half of this work on Indians. The work done in Europe may be applicable to this country also, but is only approximately so, as conditions of life, living, food, climate and other things are vastly different. I regret to mention here that the men in charge of the departments of physiology in the various medical colleges in this country who should have been the pioneers in this research for the improvement of the health of the nation have done very little in this respect.

Actual food requirements of an average Indian have still to be enquired into. For example, how much proteins and fats are necessary? It is known that it is absolutely necessary that at least part if not the whole—of these substances (proteins and fats) should be of animal origin, but no steps are taken to popularize this knowledge. Again, the value of fat is in its vitamin A content, which is usually absent from all vegetable fats and oils. I am amused sometimes to see advertisements of vegetable ghee slating that it has vitamin D added to it, whereas there is no mention of vitamin A which is more essential in fats. This shows the ignorance prevailing all around.

Other questions waiting for investigation are the detailed composition and caloric value of the various Indian articles of food and other questions like diet balance, effect of fatigue on diet and other allied questions.

Then one question waiting for solution is the purity of Indian food. It is common knowledge that it is impossible to secure pure ghee, pure milk and other articles. There is a Food Adulteration Act, no doubt, but it is only known for its inapplicability and ineffectiveness. How can our children prosper if they cannot get a minimum quantity of pure milk but it needs no repetition from me that it is impossible to obtain at present.

I will give only one example. In England, even those labourers and workers who are doing hard work are given free milk during lunch hours—for example welders, but here even our little infants and the sick and the wounded cannot get enough of that precious article, much less our labourers. Then again in England during war time bread is being issued re-

inforced with vitamin A. Who has ever thought of such or similar other measures in this land of ours?

I have, I think, now said enough to show the importance of studying the problems of nutrition as they affect this land.

The problems of Public Health are better known to all and require no great treatment in detail by me. The importance of prevention rather than cure is being realised more and more and prevention brings us to the question of Public Health. At present as is well known, the health officers are more of head scavengers than health officers. They have no powers of initiative or doing good to the public, but harm they can do a lot. The School Health Officers have a task, which is beyond them to perform. The Government appointed a Medical Reorganisation Committee somtime ago, but its report has been placed in the cold storage, even though it contained several very important recommendations, which might have led to greater efficiency and better medical aid to a greater number of people at a less cost. I hope it is not yet too late to revive that report and bring into effect at as early a date as possible even though the Government is preoccupied with the present devastating war. In this connection, I may bring to your notice the following resolution passed at the last (XIX) All-India Medical Conference held at Patna in April 1943:—

"That this Conference is of opinion that as each individual in this country has the right to obtain every type of medical service, preventive and curative, general and specialist, domiciliary and institutional, the State as well as various political parties in the country should devise ways and means to secure the same for him at an early date. This Conference also urges upon the Indian Medical Association, which must play an essential part in the preparation of what is the most important charter of health ever conceived for this nation, to render every assistance in their power towards the evolution and fruition of such a scheme."

A sickness insurance scheme is another crying need for this country. The Government of India has appointed Professor Adarkar to draw up a scheme, but it is very limited in application and scope and hardly touches even the fringe of the problem, and does not and cannot meet the demands of the country. Unless some scheme is drawn up now, even the war-returned soldiers who will settle in village farms or other peace industries, and who will have become used to modern and up-to-date treatment in the well equipped military hospitals will not be satisfied with the crude facilities available at present to people in their positions. This will naturally result in dissatisfaction. I hope the matter will be considered from this and other points of view.

And when all is said and done the whole problem rests on the question of nutrition of the populace and that question has not even begun to be studied. I think, it is time that immediate attention was focussed on this problem and a small Technical Committee of 10 to 15 members was appointed for the purpose at as early a date as possible. I would suggest a constitution for the Committee on the following lines:—

1. The Director of Public Health, U. P., Chairman.
2. Professor of Physiology Medical College Lucknow.
3. Professor of Physiology, Medical College, Agra.
4. Either Inspector General Civil Hospitals, U. P. or a representative of his department.
5. A senior officer of the Department of Public Health who has specialised or has knowledge of the problems of Food and Nutrition.

6 & 7. Professors of Midwifery and Gynaecology of the two Medical Colleges at Lucknow and Agra.

As the problem of Nutrition is of special importance from the point of view of infants and expectant and nursing mothers.

8. A lady doctor who has wide experience of the problem as it affects the public—I would suggest Dr. B. Thungumma, F.R.C.S., of Benares.

9, 10 & 11. Three representatives of the Indian Medical Association, U. P. Provincial Branch.

The names will be submitted if desired by the Government.

N.B. The Government can add one or two more members, if necessary, specially if any experts are available on the subject either in U. P. or even outside it.

The terms of reference are detailed in this note above.

I hope the matter will be considered with the seriousness and urgency that it deserves and no further time will be lost in appointing the Committee at as early a date as possible.

Lucknow.

H. N. SHIVAPURI, M.B., B.S.,
Captain, I.M.S. (Retd.)

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